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PROBLEM OF ACCELERATIONS IN AVIATION MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 27 Jul 81) pp 4-7

[Article by P. V. Vasil'yev and S. A. Gozulov]

[Text] The problem of effects of accelerations (G force ["overload"])* on an organism, particularly on a pilot's work capacity, continues to be one of the pressing problems of aviation and space medicine [1, 2].

Theoretical interest in this problem and its practical implications acquire new content and urgency at each new stage of technological development of aviation.

The search for further increase in the body's resistance to accelerations and, consequently, increase of pilot's work capacity require basically new approaches. The increasing diversity of inflight tasks and complexity of interaction in the pilot-aircraft-environment system make it imperative to examine many traditionally physiological questions from the standpoint of the systems approach and with consideration of ergonomic aspects of this problem.

The accelerations inherent in aircraft flights are divided into two main types: prolonged (piloting), which occur when maneuvering the aircraft, and impact, which occur during ejection, opening of the parachute, landing of the pilot, as well as forced ("rough") landings of the aircraft.

The effects of these accelerations on pilots differ appreciably.

As applied to piloting accelerations, the main aspects of the systems approach can be reduced to the following: flight-methodological--consideration of accelerations as one of many flight parameters; physiological--studies of effects of accelerations on various functional systems and resistance of the body as a whole; psychophysiological--studies of pilots capacities with respect to perception, evaluation and holding to the required parameters of acceleration, as well as professional performance; psychological--evaluation of pilot's attitude toward flights involving exposure to accelerations and operating protective gear; medical--screening, expert certification and dynamic observation of flight personnel; methodological-technical--refinement of anti-G gear, adjustment of the pilot's work place and aircraft control systems to provide for optimum human performance in the presence of accelerations.

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*In aviation medicine, in addition to the term, "acceleration," wide use is made of the term "G force" [overload in Russian], which indicates the ratio of body mass at earth's gravity to body mass when exposed to accelerations.

Accelerations as a parameter of flight during performance of complicated aerobatics characterize, on the one hand, the tactical and technical capabilities of the aircraft and, on the other hand, the capabilities of the pilot, so that it is imperative to use them to make an overall assessment of the efficiency of the aircraft-pilot system.

The physiological aspects of effects of accelerations on pilots have been studied the most thoroughly [3-5]. However, the vast majority of studies are concerned with the effects of single and relatively brief exposure to accelerations in the head-pelvis direction, where the chief criterion for assessing endurance is occurrence of functional visual disorders of the gray film type. As we know, when performing complicated maneuvers, these symptoms precede more serious physiological disturbances and, consequently, enable the pilot to take steps to prevent marked impairment of work capacity. With regard to the study of effects of considerable accelerations for long periods of time, there is a need to assess pilot endurance of piloting accelerations during actual flights. It is important to take into consideration not only the immediate effects, but long-term sequelae, i.e., to study problems of cumulative effects, identify the pathogenesis of the observed disorders and develop methods of preventing them.

The psychophysiological direction of investigation of the effects of accelerations on pilots (as an informative factor referable to flight dynamics) began to develop only in recent years. The principal routes for solving this problem are referable to simulation of the set of conditions under which a pilot performs on dynamic simulators with the use of recurrent modes of accelerations.

Studies of accuracy of perception and reproduction of various parameters of accelerations on a centrifuge demonstrated that man has a rather satisfactory system for gauging the magnitude and speed of changes in accelerations on the basis of his own sensations (without an accelerometer). According to R. A. Vartbaronov, mean psychometric pilot error in determining magnitude of G forces constituted ±0.5 units, while the thresholds of differential perception of G forces constituted ±12%. There were individual differences in accuracy of pilot perception of magnitude of G forces [6]. It may be assumed that expansion of research in this field will yield new data on criteria of pilot resistance to complex forms of piloting accelerations and make it possible to use psychophysiological parameters to assess work capacity.

The medical direction involves development of ways and means for a scientifically validated approach to screening pilots for new aviation equipment, expansion of the system of preventive measures, scientifically validated regulation of flight work, stricter standards of piloting accelerations and further improvement of the process of dynamic observation of flight personnel. Numerous studies conducted in this field have shown the substantial importance of individual anatomical, physiological and psychological distinctions of pilots, which determine a wide range of fluctuation in resistance to accelerations. To some extent, resistance also depends on such concomitant factors as vibration, altered ambient temperature and atmosphere, noise, fatigue, etc. For this reason, the problem is advanced of studying the combined effect of accelerations and a number of other flight factors on pilot endurance of recurrent piloting accelerations.

The psychological aspect of effects of G forces on pilots has been little-studied thus far. It should deal with the following issues: psychological conditioning of pilots for sizable accelerations; formation of deeply deliberate positive attitude of pilots to the use of anti-G equipment and knowledgeable operation thereof; development in flight of purposeful behavioral reactions that aid in preventing or attenuating visual disorders, as well as preventing illusions related to accelerations.

All these questions have a direct bearing on efficient flight performance, and they require considerably more attention on the part of aviation physicians, particularly in view of the continued refinement of aviation technology.

The medicotechnical aspect of the problem of piloting accelerations, which is aimed at optimizing pilot work capacity, is being solved through scientific research in the three following main directions: development of new ways and means of protecting pilots against accelerations [7-9]; upgrading the construction of traditional anti-G gear to improve its efficacy [10]; increasing resistance to G forces by widening the angle of inclination of the back of the pilot's seat [11-13], and others.

It should be noted that some progress has been made in all of these directions. The combined use of protective equipment and methods could yield the best effect, and it is both desirable and necessary to continue research in this direction. However, basic difficulties arise when one tries to study the practical compatibility of developed protective equipment with other systems and purpose of the aircraft. The principles of ergonomicity of the pilot-aircraft-environment system could be disrupted.

Studies of the effects on pilots of brief (impact) accelerations, which occur in emergency landings or forced abandonment of the aircraft, constitute an independent problem in physiology of accelerations in aviation.

The effects of impact accelerations in the head-pelvis direction merit special consideration, since they are related to the possibility of traumatic injuries to the spine and subsequent grounding of pilots.

The probability of vertebral trauma in such cases depends on resistance of the bone system, characteristics of accelerations involved, constructive and dynamic distinctions of the ejection seat.

Man's resistance to impact accelerations in the head-pelvis direction is determined primarily by the dynamic strength of his skeletomuscular system and, first of all, the spine.

Dynamic strength of the spine varies in different people. It depends on mineralization of vertebrae and the individual's age [14].

Estimates and indirect studies revealed that the same magnitude of acceleration can elicit a vertebral fracture in one person and have no appreciable effect on another. Resistance of the spine to accelerations is governed by a statistical law of distribution, which is close to normal, in different people. For this reason if one considers permissible a magnitude of accelerations for ejection from an aircraft that has been tested on stable subjects, one can expect a certain percentage of trauma among those whose individual distinctions are characterized by diminished resistance. Thanks to medical back-up measures for safety of ejection, the possibility of spinal trauma has been reduced to a minimum. However, the problem of setting standards for impact accelerations during ejection is still a pressing one; in essence this is a matter of having man's capabilities as a biodynamic system conform with the requirements and necessity referable to technical considerations.

To solve this problem, one must either lower ejection accelerations or conduct special screening of pilots with individual resistance to G forces.

It is quite apparent that the latter approach cannot be considered satisfactory from the practical point of view. The difficulties involved in individual screening are referable to the possible conflict between an individual's high capacity for flight work and the need to "eliminate" him from the group of applicants for flying schools due to low resistance to impact G forces. Evidently, the alternative approach to this problem is not entirely valid.

Apparently, this problem must be solved by means of further refinement of individual protective gear or development of more effective rescue equipment, which precludes the effects of traumatic accelerations in the head-pelvis direction. A certain reserve for enhancing resistance of the body in the ejection seat-pilot-G force system is related to optimization of the physical characteristics of G force proper and, first of all, its magnitude, duration and rate of build-up. It is known that G forces of the same magnitude, but differing in duration and build-up rate, can increase or decrease the incidence of traumatic injuries. The significance of characteristics of impact accelerations to occurrence of vertebral fractures during ejection lies, in particular, in the reaction of the human body, which has the mechanical properties of an elastic-shock absorbing system with its own frequency characteristics.

Such interaction can be manifested both by an increase in G force to the human body and decrease, depending on the coefficient of the body's dynamic reaction. For this reason, in order to lower the probability of sustaining trauma during ejection, it is imperative to investigate and use for optimization of effects the possibility of lowering the G force by reducing the dynamic reaction of the human body, with retention of the necessary overall energy to eject the seat.

It is of deciding importance for the pilot to maintain a specific position in the chair during ejection involving G forces in the head-pelvis direction. It is known that occurrence of spinal trauma is related to the magnitude of local pressure on the head of a vertebra. A nonuniform load on one part of the vertebra (for example, anterior edge due to a pilot's bending forward during ejection) will increase traumatism. For this reason, the dynamic reaction as a function of elements of immobilization, uniform distribution of the load over the bearing structures of the body acquires much importance. This direction of lowering traumatism has been the most studied.

At the present time, various devices are used to immobilize a person in the optimum position in the ejection seat. Molded seat backs, various modifications of seat belts, holders and other devices have been described [16, 17]. Their purpose is to prevent flexion of the spine in the thoracic and lumbar region, preclude edge stress in the anterior parts of the vertebrae and lower traumatization thereof.

Thus, the problem of piloting and impact G forces in aviation requires further investigations on the basis of a combined approach to the study of the body's capacities, refinement of means to enhance its resistance and latent reserves for optimizing the pilot-aircraft-environment system.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

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SLEEP, CIRCADIAN CYCLES OF PHYSIOLOGICAL FUNCTIONS AND PARAMETERS OF HUMAN WORK CAPACITY ON FIRST DAY AFTER CHANGING FROM ALTERED TO USUAL SLEEP-WAKING CYCLE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 19 Aug 81) pp 8-13

[Article by A. N. Litsov]

[English abstract from source] Twelve male test subjects, aged 28 to 40, took part in the studies, in which a normal work-rest cycle was preceded by three types of an altered cycle, to investigate their adaptation-readaptation reactions. The return to the normal work-rest cycle was accompanied by slight changes in physiological functions, work capacity and sleep patterns. The level of these changes was correlated with the type of altered work-rest cycles and with the degree of men's adaptation to them. The return to the normal work-rest cycle proceeded more readily, if adaptation to an altered cycle was incomplete. It is concluded that the required level of work capacity of men that have to vary their work-rest cycles frequently can be maintained by short-term (for 1 to 3 days) cycle alterations.

[Text] It is known [1-3] that the work of representatives of some occupations (pilots, seamen, operators and others) sometimes requires a periodic change in sleep-waking schedule and subsequent return to the initial schedule for the day.

The results of special studies [2-7] revealed that the phasic changes in work capacity, state of physiological systems and sleep patterns of man that occur under such conditions are attributable primarily to nonsimultaneous changes in different parameters (principle of successive and selective reaction), in accordance with the new schedule, and they are related both on the extent to which the schedules are shifted and split, as well as duration of altered schedules.

Unfortunately, most published works have been concerned primarily with the distinctions of the process of man's adjustment when changing to different variants of altered sleep-waking schedules and, to a lesser extent, returning to the initial schedule for the day [4-7]. However, according to the findings, returning to the initial sleep-wakefulness schedule can also be characterized by marked deviations of functional state and work capacity in a number of cases, and could affect the reliability and efficiency of man's performance [5-9].

Our main objective here was to consider some of the distinctions of the adaptation-readaptation process in man when he changes from different variants of altered sleep-waking schedules to the customary one, as well as to work out recommendations on the principle of constructing daily cyclograms of operator performance under such conditions.

Methods

We conducted the studies in a small chamber with artificial light and normal gas composition of air. A total of 12 men 28 to 40 years of age participated in this study; they had undergone a complete physical and were deemed to be in good health. Before changing to the customary daily schedule, the subjects used one of three variants of altered sleep-waking cycles for 6-8 days. The first schedule before returning to the usual one (1st group) involved single alternation of sleep-waking cycles over a 24-h period (sleep from 0500 to 1400 hours), the second (2d group) two such cycles (sleep from 1000 to 1600 and from 2300 to 0100 hours) and the third (3d group) three cycles (sleep from 0800 to 1100, 1400 to 1700 and 2200 to 0100 hours).

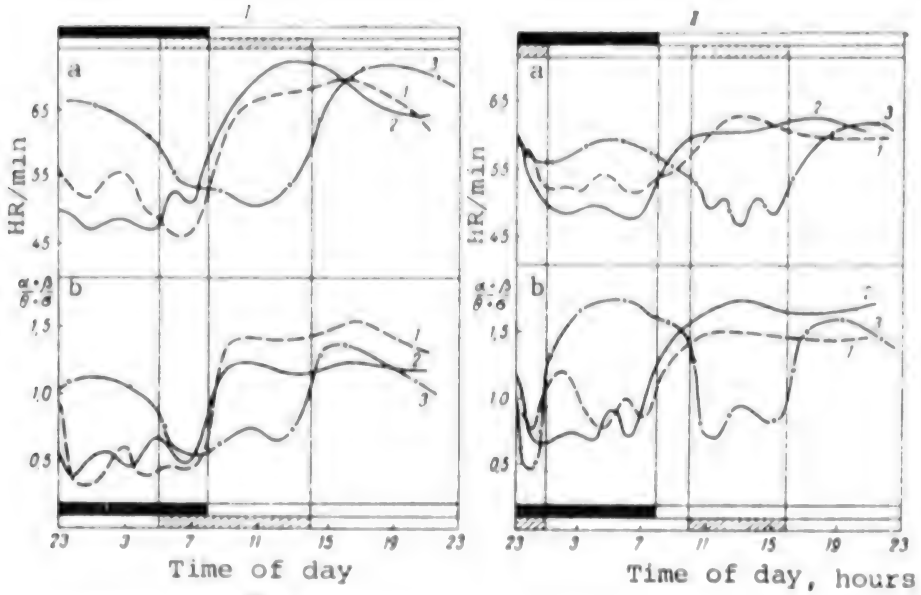
The 1st group of subjects (3 men) changed back to the usual schedule after the waking period had been reduced to 9 h (from 1400 to 2300 hours), the 2d (4 men) after reducing the waking period to 7 h (from 1600 to 2300 h) and the 3d (5 men) after shortening the waking period to 6 h (from 1700 to 2300 h).

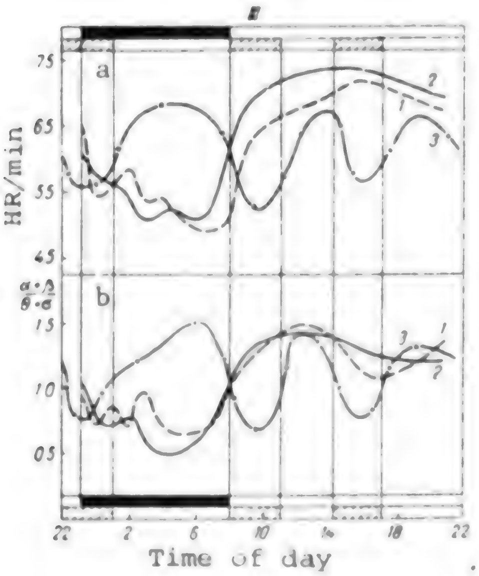
The activities of all subjects in the chamber were the same, and they were strictly regulated on a 24-h schedule, which included work (8 h), physical exercise (3 h), self-service operations (5 h) and sleep (8-9 h).

In the course of the studies, we recorded parameters of work capacity (latency periods of simple and complex motor reactions; time spent on solving arithmetic problems; accuracy of reproducing 20-s intervals), sleep quality and duration (according to EEG data and subjective estimates, supplemented with information about pulse and respiration rate), circadian pattern of heart rate (HR) and correlation between fast and slow EEG components.

Results and Discussion

In the 1st group of subjects, we studied the distinctions of adaptation and readaptation to a change to similar schedules with one cycle of sleep and wakefulness. According to the data obtained, there was gradual change in dynamics of most parameters in this group of subjects on an altered schedule (6-h shift), similar to the fluctuations that occur on the customary schedule. Thus, by the 7th-9th day on the altered schedule, a typical pattern of daily fluctuations of HR and EEG (see Figure, I, a and b) was inherent in this group of subjects, with maximum values in the middle of the waking period and minimum during sleep; higher parameters of sensorimotor reactions in the middle of the waking period (Table 1, b), as well as good sleep--they fell asleep rapidly, presenting minimal motor activity, normal distribution of slow-wave and rapid sleep phases and total duration thereof of about 7 h (Table 2, b).





Daily dynamics of HR (a) and correlation between fast (α+β) and slow (θ+σ) EEG rhythms (b) in subjects of the 1st (I), 2d (II) and 3d (III) groups (mean data). Black segments--sleeping time on usual schedule, cross-hatched--on altered schedule

1) 1st day of usual schedule
2) background data
3) last day of altered schedule

Immediately after changing to the usual schedule (sleep from 2300 to 0800 hours), most subjects presented considerable worsening of qualitative and quantitative characteristics of sleep (Table 2, c), as manifested by longer time required to fall asleep, up to 40-60 min, as well as intermittent sleep with relative increase in superficial phases and high motor activity. HR and EEG parameters were characterized, on the one hand, by coincidence of daily curves (see Figure, I, a and b) with background ones and, on the other hand, some increase of HR during sleep and EEG parameters in the waking period. In this group, there were insignificant changes in parameters of mental productivity. As can be seen in Table 1, c, some worsening of the tested parameters (simple motor reactions, arithmetic problems and timing tests) was observed only by the 10th hour of the waking period, with general retention of typical dynamics at other times of the day.

Table 1. Dynamics of subjects' work capacity with change from usual to altered alternation of sleep and wakefulness and back to usual (mean data)

Parameter	Group											
	1				2				3			
	a	b	c	d	a	b	c	d	a	b	c	d
Latency periods of simple motor reaction, ms	178	169	145	223	209	230	198	229	239	215	171	218
	154	139	120	221	180	256	196	203	248	230	217	221
	174	142	172	220	228	230	266	233	277	199	169	204
	169	141	138	226	214	230	216	170	220	175	244	247
Latency periods of reaction of choice, ms	350	340	338	403	459	467	499	437	393	374	337	383
	310	299	309	405	488	479	482	465	382	361	334	363
	326	326	313	380	487	494	491	472	381	348	354	388
	364	317	320	378	482	468	447	467	374	341	363	391
Arithmetic problem-solving time, s	4.0	3.0	3.3	4.4	4.2	3.2	3.2	4.6	3.3	3.4	3.0	4.0
	3.7	3.1	3.2	4.1	4.2	3.4	3.2	3.9	3.4	3.4	2.8	3.9
	4.2	3.1	3.1	4.6	4.4	3.4	3.8	—	3.9	3.4	2.9	3.9
	4.3	3.2	3.3	4.3	4.4	3.2	3.1	4.2	3.3	3.1	2.8	3.8
Error in reproduction of 20-s intervals, s	0.7	2.0	0.5	3.5	1.6	2.9	2.4	2.7	1.1	1.4	1.2	2.2
	1.1	2.0	1.2	2.4	0.9	2.9	2.6	1.7	3.8	1.9	1.1	1.4
	1.0	1.4	1.0	2.9	2.5	2.9	3.2	1.9	2.1	1.9	1.1	2.5
	1.9	0.9	0.8	3.4	1.4	2.5	2.6	2.7	1.3	2.7	1.4	1.6

Note: Four values are given for each parameter, which correspond to the 1st, 5th, 10th and 15th h of wakefulness

Here and in Table 2:

a) 1st day of altered schedule
b) last day of altered schedule
c) 1st day after returning to usual schedule
d) control

Thus, according to the findings for the 1st group of subjects, it can be concluded that some of the recorded parameters (spectral EEG characteristics, most psychophysiological tests) were synchronized with background data already on the 1st day after returning to the usual sleep-waking schedule, while others (HR and sleep patterns) presented mild deviations from background data, which were related chiefly to a change in the daily stereotype.

In the 2d group of subjects, we studied the distinctions of the adaptation-readaptation process with initial use of a schedule with two sleep-waking cycles. According to the findings, the HR and EEG curves (see Figure, II, a and b) presented two distinct peaks by the 6th-7th day of altered schedule, although there was slight difference between parameters recorded in the daytime and at night. The dynamics of sensorimotor tests, which presented minor deviations (see Table 1, a and b), became virtually synchronous with the new sleep-waking rhythm, while the sleep pattern during the main period (from 1000 to 1600 hours), as well as total duration and structure of sleep (see Table 2, b), were close to the usual background data, whereas in the second period (from 2300 to 0100 hours) they were still inadequate, both qualitatively and quantitatively.

Table 2. Results of studying sleep patterns of subjects with change from usual alternation of sleep and wakefulness and return to usual (mean data)

Parameter	Group											
	1				2				3			
	a	b	c	d	a	b	c	d	a	b	c	d
Falling asleep, min	8.3 — —	22.7 — —	46.6 — —	18.0 — —	19.0 45.0 —	18.6 47.8 —	68.0 — —	22.0 — —	23.0 38.0 32.0	33.2 45.0 16.6	21.1 — —	16.6 — —
Duration of sleep, % of scheduled time	71.7 — —	86.7 — —	73.0 — —	90.6 — —	51.0 54.1 —	80.6 43.2 —	48.0 — —	83.3 — —	68.8 80.5 81.7	71.2 44.3 75.5	83.2 — —	87.5 — —
Calm 5-min rest periods, %	61.2 — —	71.7 — —	56.9 — —	63.7 — —	45.8 30.1 —	60.4 44.0 —	37.5 — —	55.3 — —	50.0 60.9 59.2	50.4 46.6 52.6	58.6 — —	63.6 — —
Motor activity per hour	4.4 — —	5.0 — —	5.1 — —	5.1 — —	6.9 9.0 —	6.1 8.5 —	8.4 — —	6.3 — —	5.3 4.7 4.9	7.2 8.6 6.6	4.7 — —	4.9 — —
Superficial slow-wave EEG stages, %	60.4 — —	57.5 — —	66.0 — —	44.0 — —	69.8 86.3 —	58.1 91.6 —	69.0 — —	52.0 — —	94.4 81.9 76.3	71.2 76.7 50.0	59.4 — —	52.9 — —
Deep slow-wave EEG stages, %	29.4 — —	29.2 — —	20.8 — —	35.8 — —	20.8 13.7 —	25.8 8.4 —	23.5 — —	27.3 — —	5.6 13.6 19.1	15.0 10.0 35.0	26.8 — —	23.8 — —
Paradoxical phase, %	10.2 — —	13.3 — —	13.2 — —	20.2 — —	9.4 0 —	15.8 0 —	7.5 — —	20.9 — —	0 4.5 4.6	13.8 13.3 15.0	13.8 — —	23.7 — —

Note: Three values are given for each parameter, which correspond to the first, second and third sleep cycles.

According to the data in Table 2, the change back to the usual sleep-waking schedule elicited a significant increase in falling asleep time and general change in sleep structure in this group of subjects, in the direction of prevalence of superficial phases, as well as drastic reduction of total sleep time. There were distinct changes in dynamics of daily HR and EEG curves in this group. As can be seen in the Figure, II, a and b, on the 1st day after changing to the usual schedule, the curves of these functions were shifted in the direction of activation at night and decline during the waking period, which is indicative of signs of marked desynchronization [2, 7, 8]. The parameters of mental productivity (see Table 1, c), were characterized in this period by some smoothing of most of them and minor deviations from background data.

Thus, the changes observed after returning to the usual schedule were more significant in the 2d group of subjects than the 1st, and this was also reflected in the dynamics of well-being and work capacity.

We studied transitional processes in the 3d group of subjects with initial use of a schedule with three sleep-waking cycles. According to the obtained data, there was, on the one hand, a "new" rhythm of daily HR and EEG curves (see Figure, III, a and b) and, on the other hand, some smoothing of HR and EEG parameters, particularly in the daytime hours, in this group of subjects by the 7th-9th day of the altered schedule. There was more drastic worsening of parameters of higher nervous activity (see Table 1), with signs of subjective discomfort. Most of the subjects fell asleep more slowly in two out of the three periods, sleep was intermittent with high motor activity and of short duration (see Table 2). After the subjects changed back to the usual schedule, the dynamics of most tested parameters were essentially similar to the background values. Thus, we see in Table 2 that the qualitative and quantitative characteristics of their sleep were close to background values and considerably better than on the altered schedule. They fell asleep within no more than 20-30 min; sleep was uninterrupted, with minimal motor activity and typical distribtuion of slow-wave and paradoxical phases. The curves of daily HR and EEG dynamics also coincided with background data (see Figure, III). As can be seen in this figure, the curves distinctly follow the rhythm of the usual schedule, with only minor deviations in the early daytime hours. Approximately the same deviations were noted in dynamics of psychophysiological tests. Table 2 shows that work capacity parameters were poorer in the morning than in the daytime in this group of subjects. Only the third period was an exception, and it corresponded to the end of their professional activities.

Thus, the marked changes observed at the end of the period of altered schedule in dynamics of most physiological functions, parameters of work capacity and sleep (reflecting incomplete adjustment) disappeared immediately after returning to the usual schedule in the 3d group of subjects. This is indicative of the fact that it was relatively easy for this group of subjects to return to the usual sleep-waking schedule, as compared to other groups.

To sum up our findings, it can be concluded that the return to the customary alternation of sleep and wakefulness after being on an altered schedule is associated with relatively minor deviations of dynamics of physiological functions, work capacity and sleep parameters. The magnitude of these deviations is closely related both to the type of schedules used and extent of operator adaptation to them.

As shown by the results of investigations, the most stable changes in the parameters studied under these conditions were observed only in HR dynamics and sleep pattern, which reflect more than other functions the level of wakefulness and current state of the body's circadian system [2, 6, 9].

It was noted that the process of readaptation is considerably easier for subjects who did not adapt completely to a new sleep-waking schedule (3d group) and relatively slow when adaptation was virtually completed (1st and 2d groups). This shows that the previously developed sleep-wakefulness stereotype is more stable than a newly formed one [9-13], as well as the existence of a dependence of deviations occurring upon return to the usual schedule on extent of man's adaptation to a new sleep-waking schedule [9, 14, 15]. According to our findings, man retains the capacity for rapid restoration of initial level of circadian rhythm of his functional state and work capacity for some time after changing to a different schedule. This distinction of the body's reaction to a change in sleep-waking schedule is apparently a biologically significant pattern, which is related to the presence of special adaptations developed in the course of long-term evolution, which provide for economically desirable adjustment of the body to cyclically changing environmental conditions. Apparently, these patterns can explain the findings of these studies concerning relatively easy change to the usual sleep-waking schedule, particularly when the old stereotype has not yet been replaced with a new one.

On the basis of our data, it may be assumed that brief (up to 1-3 days) use of an altered daily schedule is the optimum way for maintaining the required level of professional work capacity of man when there are frequent changes in sleep-waking state schedule [14, 15].

Our results may be useful to development of daily cyclograms of performance of specialists working in a unique habitat, as well as to evaluation of optimality of work and rest schedules that require frequent changes in sleep-wakefulness cycles.

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ROLE OF HORMONAL COMPOUNDS IN REGULATION OF ELECTROLYTE METABOLISM IN THE PRESENCE OF EMOTIONAL STRESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 8 Apr 81) pp 13-16

[Article by B. V. Afonin, L. L. Orlov, N. F. Kalita, T. A. Viting and R. A. Tigranyan]

> [English abstract from source] The emotional stress simulated by examinations taken by medical students led to a decrease of sodium concentration in blood. This was a result of a simultaneous increase of mineralocorticoids and a decrease of glucocorticoids responsible for sodium concentration in blood. Both inhibition of glucocorticoids and stimulation of mineralocorticoids were associated with a high activity of plasma renin and a low concentration of adrenocorticotropic hormone.

[Text] The state of metabolism under emotional stress has long since drawn the attention of researchers specializing in aviation and space medicine. Processes of excitation of nerve, muscle and any other tissue are associated with shifting of Na in cells and discharge of K into intercellular space [1]. Emotional stress is characterized by excitation of various systems of the body [2], which could be the cause of electrolyte changes [3]. Changes in electrolyte metabolism may also be secondary, as a result of elicited changes in electrolyte metabolism and excitation of the hypophyseoadrenal and renin-angiotension-aldosterone (RAAS) systems, which are involved in regulating electrolyte homeostasis in the body.

Our objective here was to study the role of the RAAS, as well as adrenocorticotropic hormone (ACTH) and cortisol, in regulating electrolyte metabolism under emotional stress, as it relates to problems of aerospace medicine.

Methods

We conducted the studies on 15 medical students (men), 28-35 years of age, under emotional stress elicited by taking a test. We took blood samples and analyzed them just before the beginning of a test and immediately after passing it well. Such a set-up was felt to be the only possible one to study expressly emotional stress, since the main condition was that the students did not know about our study in advance. Aldosterone, ACTH and cortisol of blood, as well as plasma renin activity were determined by radioimmune analysis using Cea-Ire-Sorin (France) kits; electrolyte (Na, K, Ca and Mg) concentration in blood was assayed by atom-absorption spectrophotometry; arterial pressure (AP) was measured by the method of Korotkov, minute (MV) and stroke volume (SV) of the heart were determined by echocardiography. The obtained data were submitted to processing by the method of variational statistics.

Results and Discussion

Emotional stress, caused by anticipation of taking a test, was externally manifested in most students by some inhibition and insignificant autonomic reactions (pallor of the integument, hyperhidrosis of the palms, slight tremor of the fingers, dryness of the mouth), and more frequent micturition in some cases. In the pretest period, the students demonstrated elevated AP (systolic pressure 147.0±2.12 mm Hg, diastolic 93.5±2.7 mm Hg), increase of MV and SV.

Table 1. Effect of emotional stress on plasma renin activity (in ng/mℓ/h), concentration of ACTH and aldosterone (pg/mℓ), cortisole (μg/ℓ) and Na (meq/ℓ) in blood

Blood sample taken	Renin	Aldosterone	ACTH	Cortisol	Na
			a		
Before test	10,9±1,8	68,1±12,2	51,3±10,9	194±28	141,5±1,8
After test	18,0±2,3*	77,1±12,9	46,0±9,6	227±22	137±1,2
			b		
Before test	9,7±1,8	71,3±20,5	52,3±10,9	194±28	142,2±1,6
After test	22,1±2,9**	90,7±19,6	46,0±9,6	167±22	137±1,8
			c		
Before test	10,3±2,3	76,1±12,3	36,4±8,2	213±28	142,2±2,2
After test	18,9±3,0*	87,1±12,9*	34,6±7,1	175±26	137,0±2,4

Key: a) change in tested parameters in all students (n = 15)
b) change in tested parameters in subjects who reacted by an increase in renin activity (n = 12)
c) change in tested parameters in those who reacted by an increase in aldosterone concentration (n = 11).
Here and in Table 2: *P<0.05, **P<0.01.

The results of assaying blood electrolytes just prior to the test showed significant changes in concentration, as compared to the conventional norms, although Na and Mg were demonstrable at the bottom and Ca at the top of the conventional range. Analysis of blood hormone levels in this period revealed plasma renin activity that was considerably greater than normal (Table 1a), whereas concentration of ACTH, aldosterone and cortisol in blood did not exceed the range of normal fluctuations (see Table 1a).

After passing the test successfully, the students' well-being improved, emotional inhibition disappeared, although autonomic reactions (hyperhidrosis of the palms and tremor of the fingers) remained. They were also moderately thirsty. After the test, AP dropped to normal levels, constituting 127.0±0.32 mm Hg for systolic pressure and 77.0±2.16 mm Hg for diastolic; MV and SV diminished; however, they did not reach normal levels.

Table 2. Effect of emotional stress on plasma renin activity (in ng/mℓ/h), concentration of ACTH and aldosterone (in pg/mℓ), cortisol (μg/ℓ) and Na (meq/ℓ) in blood

Blood taken	Renin	Aldoster.	ACTH	Cortisol	Na
			a		
Before test	11,1±2,1	61,6±22,2	58,0±13,3	198±30	142,6±1,8
After test	18,1±3,2	72,8±12,2	47,0±12,9	153±20	133,7±1,2••
			b		
Before test	10,3±2,6	81,6±25,6	48,1±10,9	201±26	137,0±2,6
After test	19,4±3,8•	90,2±16,3	28,4±5,15	128±9••	136,9±2,9
			c		
Before test	7,9±2,1	84,2±26,0	63,8±11,7	212±29	141,3±2,9
After test	19,9±3,7••	78,8±17,2	42,6±14,8	126±10••	131,0±1,7•

Key: a, b, c) change in tested parameters in subjects who reacted by a decrease in concentration of Na (n = 11), ACTH (n = 9) and cortisol (n = 9)

Studies of electrolyte content of blood, which were conducted at this time, revealed some decrease (as compared to pretest level) in concentration of Na (see Table 1a); there were negligible changes in K, Ca and Mg levels in blood. Such a state of electrolyte metabolism corresponded to even greater (as compared to pretest level) activation of plasma renin; blood aldosterone and cortisol levels presented some tendency toward rise, whereas ACTH concentration diminished somewhat (see Table 1a).

In order to determine the possible mechanisms of the above changes in tested parameters, we singled out groups of subjects who reacted similarly with regard to renin (see Table 1b), aldosterone (see Table 1c), Na (Table 2a), cortisol (see Table 2b) and ACTH (Table 2c). In students who reacted after the test by an increase in plasma renin activity (see Table 1b), there was no reliable decrease in blood Na concentration, and this could be related to the effect of renin on aldosterone concentration, which only presented a tendency toward increase in these students (see Table 1b).

In subjects who presented an increase in aldosterone concentration in blood after taking the test, we also failed to demonstrate a reliable decline of blood Na level, although the increase in aldosterone in this group of students occurred against a background of reliable increase in plasma renin activity (see Table 1c). In subjects whose reaction consisted of a decrease in blood cortisol concentration, we observed no decrease in Na concentration with concurrent reliable increase in plasma renin activity (see Table 2b). In students whose post-test reaction was a decline in ACTH concentration, we observed a reliable decrease in concentration of blood Na and cortisol, along with increase in plasma renin activity (see Table 2c). This is apparently related not only to depressed ACTH and cortisol secretion, but marked activation of plasma renin.

Thus, the decrease in blood Na concentration after taking the test occurred against a background of increased plasma renin activity and decrease in ACTH concentration; there was a less marked correlation between changes in Na and aldosterone concentrations, and none with decrease in cortisol concentration.

The high activity of plasma renin with the model of emotional stress that we used is consistent with data in the literature, which indicate that this parameter increases with various forms of stress, and this could be related to the significant role of central neuroreflex mechanisms in regulation of renin secretion, as well as the stimulating effect of catecholamines [2, 5, 6]. We cannot rule out the possibility that stimulation of renin secretion is related to a relative Na shortage, caused by excitatory processes inherent in emotional stress; in this case, activation of RAAS could withstand the changes in electrolyte metabolism [2, 7]. At the same time, activation of RAAS per se could serve as the cause of decline of blood Na level [7]. An increase in plasma renin activity is not necessarily indicative of increase in activity of the entire RAAS , since the effect of angiotensin II on aldosterone secretion may be blocked [9]. The fact that the changes in aldosterone concentration, both before and after taking the test, did not exceed the normal range, in spite of rather high plasma renin activity, could serve as a confirmation of that statement. Such dissociation could be related to depletion of the adrenal cortex, which loses sensitivity to such a high blood renin level, and this is indirectly confirmed by the concurrent decrease in blood cortisol concentration [10]. This assumption is in contradiction with our data (see Table 2c), which indicate that a decline in cortisol concentration corresponds to a decline in concentration of ACTH, which is the principal stimulator of cortisol secretion in the adrenals [10]. At the same time, there was an inverse correlation between decrease in blood cortisol concentration and increase in plasma renin activity (see Table 2b), whereas the increase in aldosterone concentration corresponded to an increase in plasma renin activity (see Table 2c). This confirms the stimulating effect of the RAAS on aldosterone secretion and its inhibitory effect on glucocorticoid secretion [10]. A decrease in glucocorticoid secretion, like increase in mineralocorticoid secretion, would cause depression of processes of electrolyte mobilization and increase processes of deposition thereof in tissues, which is perhaps the cause of decrease in blood electrolyte (particularly Na) concentration [7].

Thus, one should consider the decrease in blood Na concentration in the presence of emotional stress as the result of simultaneous increase in mineralocorticoid activity, which increases deposition thereof in tissues, and decrease in glucocorticoid activity, which causes concurrent decrease in processes of mobilization of Na from the pool; both depression of glucocorticoid secretion and activation of mineralocorticoids are related to high plasma renin activity.

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METABOLIC DISTINCTIONS RELATED TO INTAKE OF LOW-CALORIE 'SURVIVAL' RATIONS CONSISTING ONLY OF READILY ASSIMILATED CARBOHYDRATES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 4 Aug 81) pp 16-25

[Article by I. G. Popov, P. A. Lozinskiy, A. A. Latskevich and I. A. Romanova]

[English abstract from source] On the basis of the study of carbohydrate, mineral, amino acid, nitrogen metabolism, nutritional status and general health condition of test subjects, it is concluded that in the case of emergency landing in an area with a temperate climate the contingency diet consisting of 300 g of readily assimilable disaccharides can be consumed for 5 days.

[Text] Much attention is devoted to questions of emergency rations and water provisions in studies of the problem of "survival" of aircraft crews after forced landing on the ground or in water. However, in spite of progress in this area, many aspects of nutrition and water provisions in emergency situations have still not been adequately studied or developed.

There are difficulties involved with the use of small-sized portable emergency supplies (ES) [emergency kits?], in which the volume of food is very limited and there is either little or no water. The kit that has been used for a long time in aviation practice, consisting of 300 g chocolate and 60 g table salt, is an example of such ES. Like other variants, this ES is intended for 3-5-day "survival" and, consequently, partial starvation inevitably develops when it is used.

With such small ES, questions of chemical composition and nutritional value of food, as well as tactics for use thereof according to the nature of the emergency, acquire importance. The shelf life ["operating qualities"] of the products stowed in ES is also very important.

At the present time, the products and assortments of products contained in ES usually have a mixed chemical composition. Apparently, this reflects the views of many researchers, who tried to create a semblance of optimum nutrition for emergencies, balanced in protein, fat, carbohydrates, vitamins, minerals, etc. In practice, this turned out to be difficult to achieve, biochemically insufficiently warranted and, in a number of cases, led to adverse consequences. In particular, chocolate, which had become a traditional element of many ES, has several serious handling flaws and causes many remarks when used in a hot climate and when there is a water shortage. This makes it necessary to upgrade the food group of ES and use other products for such purposes, which keep well when stored for long periods of time and are more adequate to conditions of partial starvation and dehydration.

In this regard, the prospects of developing an emergency food supply consisting of readily assimilable carbohydrates, which have a long shelf life if properly packaged, merit special attention. There are some prerequisites for formulating the problem in this manner, particularly for emergencies when there are limited water resources and considerable loss of fluid. As a result of our studies, it was determined that intake of canned meat under such conditions is not desirable, due to the high osmotic activity of the nutrients it contains. For this reason, when there is a threat of dehydration, it is desirable to take carbohydrates [1].

Studies of external fluid metabolism during 10-day use of emergency rations with a caloric value of 1480 kcal/day revealed that carbohydrate-fat rations were more effective than meat and fat [2].

All this prompted us to conduct the present study in order to substantiate the hygienic permissibility of using limited amounts of readily assimilated carbohydrates for emergency "survival" for a period of 3-5 days. The results enabled us to determine that there is a possibility of replacing mixed foods in ES (chocolate, meat-fat canned goods, pemmican, etc.) with pure carbohydrates and permit a change to mononutrient diet for the limited duration of emergency conditions.

Methods

We selected two types of rations consisting only of readily assimilated disaccharides as models of low-calory, carbohydrate emergency rations. The disaccharides included saccharose, which is similar in assimilability to monosaccharides--glucose and fructose--and is widely used in our country as a food. The food was in the form of lump sugar (99.9% saccharose) and caramel (96% saccharose). The emergency food supply weighed a total of 300 g, i.e., it corresponded to the food group of ES containing only 300 g chocolate. The first ration consisted of 300 g hard caramels and the second 120 g of the same type of caramel and 180 g lump sugar. The caloric value of the first ration constituted 1076 kcal (287 g carbohydrate) and the second 1106 kcal (295 g carbohydrate). The difference in caloric value of these rations is insignificant (only 30 kcal), particularly if distributed over the duration of the emergency (5 days). Four people used the first type of rations and three, the second. Since the chemical composition of the rations was virtually the same, analysis of metabolism was made for the entire group of seven people.

It is known that intake of caramels alone for several days could become boring and cause irritation of the mucous membrane of the mouth, tongue and gums. For this reason, it was interesting to determine whether it is possible to combine caramels and sugar lumps. Due to the fact that the latter are not as hard, there can be rapid intake of readily assimilated carbohydrates, which is important if there are signs of hypoglycemia. At the same time, the addition of caramels to the rations makes it possible to use for this purpose the forms of sugar that dissolve the slowest in saliva, in order to prolong the intake of food and to appease hunger faster.

To assess emergency rations consisting of carbohydrates, we simulated one of the variants of development of an emergency situation. On the morning of the day when the studies were begun, after a medical examination on a fasting stomach, the pilots received the standard preflight breakfast. Nutritional value of the breakfast was as follows: 43 g protein, 46 g fat, 115 g carbohydrates, total of about 1017 kcal. The breakfast items had a net weight of 505 g. In addition, they were given 200 mℓ hot tea and 200 mℓ fruit juice. The "flight" began 1.5 h after breakfast, and after 2 more hours an "emergency landing" was announced. Duration of "emergency conditions" was set at 5 days. All of the subjects used only the emergency rations for 5 days following their preflight breakfast.

During the period after the "emergency landing," the subjects received drinking water at the rate of 1 ℓ per day of the study. It should be recalled that they had received an additional 400 mℓ fluid on the first day with their preflight breakfast. The subjects were advised to use water as economically as possible, but not to the extent of experiencing severe thirst and dehydration.

The mealtime schedule for the first group of subjects provided for the preflight breakfast in the morning and 20 g caramels in the evening of the 1st day; they were scheduled to take 70 g caramels on the 2d, 3d, 4th and 5th days, to be evenly divided for breakfast lunch and dinner at the usual time.

The second group of subjects had the preflight breakfast in the morning of the 1st day and 20 g sugar in the evening; they had 40 g sugar and 30 g caramels on each of the 2d, 3d, 4th and 5th days. Sugar was taken in equal amounts 3 times a day at the usual mealtime hours. The subjects consumed caramels between meals [breakfast, lunch and dinner) to appease hunger.

During tests of the rations, the start of each day was set at 0800 hours, after collecting noctural urine for the preceding day. Thus, the 1st day started at 0800 hours before the preflight breakfast and ended at 0800 hours the following day; the fifth day ended at 0800 hours of the 6th day of the study. This enabled us to monitor daily dynamics of body weight, fluid and food intake, diuresis, and to collect blood and urine specimens in accordance with the conventional practice for studying daily dynamics of metabolism and nutritional status of a healthy man.

During the period of intake of emergency rations, we studied the daily dynamics of nutritional status of the subjects on the basis of weighing them, measuring parameters of carbohydrate, nitrogen, amino acid and mineral metabolism. We analyzed the dynamics of fluid intake and diuresis. We assessed the data concerning the subjects' well-being and general condition. We recorded their reports about appetite, thirst and getting tired of the rations.

Male volunteers 35-40 years of age participated in these studies; they had undergone a physical and were deemed to be essentially healthy. There were individuals who were overweight, normal and underweight.

During the experimental period, they continued to perform their usual work, which involved mean energy expenditure of 3000-3200 kcal/day, i.e., in the range of energy expenditure referable to the first occupational group, according to the 1968 standards of the USSR Academy of Medical Sciences. In general, the subjects had a sedentary way of life, with negligible physical exertion referable mainly to mental work. The living conditions were those inherent in inhabitants of a large city. The studies were conducted in late spring, in the temperate climate zone, at comfortable ambient temperature. The choice of these conditions was attributable, in particular, to the desire to examine, at this stage, the effects primarily of a drastic change to an unusual, low-calorie carbohydrate diet with retention of former living conditions on metabolism and nutritional status.

Results and Discussion

Body weight and its dynamics constitute the conventional indicator of quantitative adequacy of nutrition. Table 1 lists data on dynamics of the subjects' weight during use of emergency carbohydrate rations for 5 days after intake of a preflight breakfast. The data are given for two "survival" terms, 3 and 5 days. According to the data in Table 1, all of the subjects continuously lost weight for 5 days; this was inevitable, since the energy they expended, which constituted 3000-3200 kcal when scaled to an average person weighing 70 kg exceeded substantially the caloric value of the food they consumed. On the 1st day, they consumed about 1090 kcal, and on subsequent days about 258 kcal. As a result, there inevitably had to be expenditure of endogenous sources of energy. At the first stage of starvation due to inadequate nutrition, there is usually expenditure of spare glycogen and amino acids from extracellular space at first. It is believed, that with a total fast the supply of glycogen is sufficient for only 1 day. In our studies, the situation was less acute on the 1st day. For this reason, the change to utilization of predominantly fat reserves should have occurred somewhat later.

As was to be expected, most subjects presented maximum weight loss on the 1st day of the low-calorie diet. Thereafter, there was less weight loss and it was minimal in most cases on the 5th day. The mean generalized data also confirm this orientation of weight dynamics.

The weight loss (percentage of base weight) was in the range of 2.71 to 4.34% in the first 3 days, constituting a mean of 3.56±0.22% for the group; it was in the range of 4.46 to 5.7%, the mean being 4.9±0.17%, for the 5-day period. In both variants of duration of emergency diet, such a weight reduction should be interpreted as not being related to significant depletion of the body's reserves and far from the critical level of 40%. We failed to detect any differences between the two types of rations with regard to weight dynamics.

The effect of the subjects' initial physical condition on dynamics and absolute parameters of body weight with the low-calorie diet merits special consideration. According to Broca's index, four subjects were overtly overweight before the study, one had an almost normal weight and two weighed less than the norm. If we were to compare the subjects' weight to the levels recommended by A. A. Pokrovskiy [3], we would find that it was above normal in all of them. After days on the low-calorie diet, 3 subjects were still overweight, according to Broca's index, one dropped to normal and 3 were underweight. This parameter was 6 and 7 kg below normal in 2 subjects whose weight was low initially. We were impressed by the fact that the same 2 subjects presented the greatest percentile weight loss, particularly after 5 days. As for the indicators of normal body weight [3], even after 5 days on the low-calorie diet, with the given energy expenditure and fluid loss, the weight of all subjects exceeded the recommended level, considering their height and constitution. All this warrants the belief that, under our experimental conditions, there was generally not significant enough weight loss to have an appreciable effect on health, work capacity and well-being of the subjects during the 3 and 5 days of intake of the tested rations. However, it should be mentioned that those whose weight was below normal according to Broca's index at the start of the emergency situation were in a worse position.

Table 1. Dynamics of subjects' weight during intake of emergency rations consisting of carbohydrates

Subject	Height, cm	Base weight, kg	Status of wt., Broca index, kg	Subjects' weight loss (kg/day) (percentage of base weight is given in parentheses), [on following days]							Weight after 5 days	Recommended normal wt., kg [3]
				1	2	3	1-3	4	5	1-5		
L-y c	184	85,35	+1.35	[illegible] (1.35)	[illegible] (2.52)	0,75 (3,40)	2,90 (3.40)	0,70 (4,22)	0,40 (4,68)	4,0 (4,68)	81.35	79.2
P-v c+s	177	84.45	+7.45	1.35 (1.60)	0,55 (2,26)	0,75 (3,14)	2,65 (8,14)	0,70 (4,00)	0,70 (4,80)	4,05 (4,80)	80.4	79.8
Kh-v c	172	77.30	+5.3	0.80 (1.03)	0.90 (2.19)	0.40 (2,17)	2,10 (2.71)	0.70 (3,62)	0,65 (5,46)	3.45 (4. 6)	73,85	69.7
L-zh c	172	77,20	+5,2	1.90 (2,46)	0.60 (3.24)	0,60 ([illegible],02)	3,10 (4,02)	0,20 (4,02)	0.35 (4.73)	3,65 (4,73)	73,55	69.7
K-v c+s	172	75,35	+3,35	0.60 (0,80)	1.10 (2.26)	0,90 (3,45)	2,60 (3.45)	0,55 (4.18)	0,40 (4.71)	3.33 (4.71)	71,8	69.7
V-ts c	178	74.85	-3.15	1.15 (1,54)	1.00 (2,88)	0,70 (3.78)	2.85 (3.78)	0.60 (4.58)	0.40 (5.14)	3,85 (5.14)	71.0	67.3
K-v c+s	168	65.70	-2.30	1.40 (2.13)	0,90 (3.50)	0,55 (4,34)	2.85 (4.34)	0,60 (5.25)	0,30 (5.70)	3,75 (5.70)	61.9	59.3

Key: c) rations consisting only of caramels (300 g)
c+s) rations consisting of caramels (120 g) and lump sugar (180 g)

The human body has a relatively small reserve of carbohydrates. It is generally considered that an average man weighing 70 kg has 45-75 g (maximum 150 g) glycogen in the liver and about 280 g in muscles, i.e., a total of 325-355 g [4]. The energy value of such a supply of carbohydrates constitutes 1219-1331 kcal. For this reason, according to the above estimates, our subjects, who were on a partially starvation diet and developed a calorie deficiency, could have exhausted their glycogen supply on the very first day. This could lead to a decrease in blood glucose content. Of course, it should be borne in mind that it is relatively rare to encounter a blood sugar drop to below normal (hypoglycemia) under ordinary living and dietary conditions. Transient hypoglycemia develops more often as a result of intensive physical labor, when the body's carbohydrate resources are depleted [5]. In the case of semistarvation, which occurred with intake of the above carbohydrate rations, there could be sporadic hypoglycemia, with [illegible] adverse consequences. In

Table 2. Blood sugar dynamics during 5 days of consumption of carbohydrate emergency rations

Subject	Wt. status by Broca index	Blood sugar, mg%												
		days on emergency rations											3d day after study	
		1		2		3		4		5		6		
L-iy	1.35	[illegible]	73	73	99	84	88	56	56	65	74	75	85	89
P-ov	7.45	78	72	78	76	96	103	72	53	88	74	78	107	69
Kh-ov	[illegible].3	[illegible]	99	59	95	95	72	80	67	55	64	60	67	86
L-ich	[illegible].2	[illegible]	79	91	70	85	103	64	64	63	79	72	107	[illegible]
K-ov	[illegible]	[illegible]	107	50	91	84	48	74	52	54	82	66	82	77
V-ets	[illegible]	[illegible]	76	68	69	79	55	70	78	58	74	74	84	97
K-ev	[illegible]	108	[illegible]	49	90	91	70	83	49	48	49	54	67	71
Group mean, M±m		[illegible]	[illegible] ± 1.90	67.00 ± 5.74	81.00 ± 4.20	87.70 ± 2.38	77.00 ± 7.70	71.30 ± 3.78	60.00 ± [illegible]	61.60 ± 5.60	71.00 ± 4.62	68.40 ± 2.52	85.60 ± 5.60	85.80 ± 2.52

Note: Fasting blood samples were taken at 0900 hours and then at 1800 hours before supper.
*Fasting, before preflight breakfast **Fasting, at end of 5th day of study

order to examine the dynamics of blood sugar levels in the subjects, we analyzed their blood at 0800 hours on a fasting stomach and at 1800 hours before supper. The results of these tests are listed in Table 2. Blood glucose was assayed by the glucose-oxidase method, in which 80-100 mg% is considered the physiological norm.

According to the data listed in Table 2, there was little change in blood glucose on the 1st day of the emergency diet, and it remained in the normal range, not less than 70 mg%. On the morning of the 2d day, 4 out of 7 subjects presented noticeable hypoglycemia, and 2 of them were underweight according to Broca's index. At 1800 hours of the same day, hypoglycemia was found in only 1 subject, who had the poorest Broca indexes.

On the morning of the 3d day, glucose level was normal in all subjects; at 1800 hours it was less than 70 mg% in 3 cases (the same subjects as in the morning of the 2d day). On the morning of the 4th day, below normal glucose levels were demonstrated in 5 out of 7 subjects, and in 3 of them this parameter was below 70 mg%, in the other 2 it was at the bottom of the normal range. On the evening of the 4th day, blood glucose levels dropped in all subjects, and it was less than 80 mg% in 6 out of 7. On the morning of the 5th day, this parameter was below normal in 6 out of 7 subjects; it remained in the normal range only in the "fattest" subject. The situation improved somewhat by the evening of the 5th day, and blood sugar was substantially below normal in only 2 subjects, and in the others it was close to the bottom of the normal range. On the morning of the 6th day, prior to termination of the studies, blood glucose was below 80 mg% in all cases, but in 4 of them it was above 70 mg% and close to the bottom of the normal range.

Thus, as semistarvation developed during intake of low-calorie carbohydrate rations, virtually all of the subjects presented sporadic hypoglycemia. Relatively more frequent and more severe hypoglycemia was demonstrated in subjects who were relatively less overweight in the base period according to Broca's index. In all of the subjects, hypoglycemia was observed relatively more often in the second half of the study period.

According to the generalized parameters, blood sugar of the entire group of subjects dropped gradually from the 1st to 5th days, but this decline was undulant.

Analysis of individual data also revealed undulant dynamics of blood glucose levels. The impression was gained that, after a sporadic drop of its level in blood, by virtue of gluconeogenesis the compensatory mechanisms restored the required blood sugar level. Continuous hypoglycemia was noted only in 1 subject after the evening of the 4th day, and he was initially underweight. At the same time, blood glucose was virtually at the base level on the morning of the 6th day in 3 subjects, and at 60 mg% or higher in 2 cases.

There is the impression that the gluconeogenesis reserves had not yet been depleted. This is generally confirmed by the parameters of dynamics of the subjects' general condition.

According to the subjects' own appraisal, they did not notice any worsening of well-being or work capacity on the 1st day on the low-calorie diet. The slight sensation of hunger, which appeared toward evening, was largely eliminated by intake of 20 g carbohydrate and a glass of cold water. Intake of warm water was lesss effective in diminishing hunger.

For the next 4 days, all of the subjects reported periodic general weakness, worsening of well-being and work capacity. The time of occurrence of these signs, as well as their duration and severity, varied in different subjects. Subjects L-y, P-ov, L-ich and Khl-ov reported only minor and brief worsening of well-being on the 4th-5th days, whereas V-ets, K-ov and K-ev complained of periodic weakness already on the 2d-3d days. This weakness increased and occurred more frequently on the 4th-5th days, particularly toward the end of the work day. Interestingly enough, the last three subjects had a lower weight and nourishment according to Broca's index. On the whole, all of the subjects assessed their condition as quite tolerable, even at the end of the 5th day on the low-calorie diet. It is important to mention that we failed to observe disturbing hunger pangs, morbid sensations referable to the stomach and intestine, headache, nausea, vertigo or other symptoms of complete starvation. Intake of small amounts of carbohydrates dulled rather effectively or eliminated entirely the sensation of hunger and improved well-being. Evidently, periodic appearance of general weakness and diminished work capacity were related to sporadic hypoglycemia. Dynamic determination of hand strength revealed that there was no worsening of this parameter and even improvement thereof by the 5th day of the study. Thus, on the average for the group of subjects, hand strength increased from 56 to 58.6 kg by the 5th day on the right and from 52.7 to 55.1 kg on the left. Backbone strength showed virtually no change on the 5th day in 4 subjects and diminished from 5 to 13 kg in 3, including the 2 subjects who were undernourished initially. On the very 1st day of the recovery period, this parameter virtually failed to differ from the base value in all subjects. During the test period, we observed some decrease in backbone strength in most subjects on the 3d-4th days. Retention or even improvement of dynamometric parameters of muscular strength on the first days of the semistarvation diet is apparently a reflection of intensification of excitatory processes due to the physiological strain of the early stage of low-calorie nutrition.

Electrocardiography revealed that a correct rhythm of cardiac contractions persisted in all of the subjects; the time intervals of the EKG (PQ, QS, QT) remained in the normal range, and there was no change in position of the axis of the heart. Amplitude characteristics of EKG waves did not undergo appreciable change. Only some subjects presented a slight decrease in amplitude of T_2 wave, and there was also some widening of QT segment. These signs could be due to changes in electrolyte metabolism and, mainly, negative balance in metabolism of macroelements on the carbohydrate diet. In this regard, the dynamics of potassium metabolism merit special attention. Arterial pressure periodically dropped by 5-15 mm Hg. The pulse periodically slowed down by 5-10/min, as compared to base values.

Table 3. Dynamics of daily excretion of macroelements in urine with intake of low-calorie carbohydrate rations

Diet	Macroelements, mg/day			
	potassium	sodium	chloride	phsophorus
Usual	2278±191	3653±388	8083±612	889±87
Low-calorie carbohydrate rations: 1st day	2070±142	2470±192	5322±782	827±76
2d "	1160±101	2638±870	2638±42	568±69
3d "	1103±152	619±140	1388±139	679±109
4th "	1001±147	528±10	1030±10	573±219
5th "	1012±127	406±73	662±167	[illegible]06±32

Studies of excretion in urine of potassium, sodium, chloride and phosphorus revealed appreciable decrease in elimination of these macroelements in all subjects from the 1st to 5th days of intake of low-calorie carbohydrate rations. According to the data listed in Table 3, there was maximum decrease in excretion of sodium and chlorides, the levels of which in urine were significantly lower by the 5th day than those observed with an ordinary diet and considered the physiological norm. Excretion of these two macroelements diminished drastically as early as the 3d day and that of potassium on the 2d day, subsequently holding at the bottom of the normal range. Phosphorus excretion remained at the bottom of the normal range, even at the end of the 5th day. Thus, with the change to a carbohydrate diet and establishment of negative balance of macroelements, already on the 2d-3d day mechanisms began to function intensively that are instrumental in reducing loss in urine of all of the tested minerals. As a result, excretion of potassium and phosphorus during the 5 days on the low-calorie diet remained at the bottom of the normal range, whereas excretion of sodium and chloride was on a level indicative of impending depletion of body salts. No doubt, the good nutritional macroelement status prior to the start of the low-calorie diet played an important part. The situation with regard to sodium, chloride and potassium could have been worse with intensive loss of fluid due to perspiration (for example, in a hot climate). In general, the supply of macroelements studied can be assessed as permissible, considering the satisfactory subjective state. The question of taking supplemental NaCl requires investigation.

Table 4. Free amino acids in blood plasma of subjects (n = 5) who were on carbohydrate rations for 5 days

Amino acids	Concentr. mg%, fasting, 0800 hours		P
	1st day	end of 5th day	
Essential amino acids			
Lysine	3,55±0,18	3,22±0,14	>0,05
Threonine	1,60±0,11	1,20±0,10	<0,05
Valine	1,98±0,08	2,13±0,11	>0,05
Methionine	0,30±0,06	0,32±0,01	>0,05
Isoleucine	0,61±0,03	1,69±0,07	<0,001
Leucine	1,21±0,10	2,66±0,12	<0,001
Phenylalanine	0,70±0,07	0,72±0,07	>0,05
Unessential			
Histidine	1,35±0,18	3,22±0,14	<0,01
Arginine	1,07±0,09	0,91±0,07	>0,05
Aspartic acid	0,03±0,01	0,27±0,04	<0,01
Serine	1,21±0,09	1,16±0,10	>0,05
Glutamic acid	0,79±0,11	1,11±0,16	>0,05
Proline	1,78±0,05	1,56±0,11	>0,05
Glycine	1,31±0,08	1,14±0,17	>0,05
Alanine	2,08±0,16	2,32±0,14	>0,05
Cystine	0,76±0,12	0,71±0,06	>0,05
Tyrosine	0,89±0,07	0,86±0,08	>0,05
Total essential amino acids (E)	9,98±0,09	11,94±0,09	<0,01
Total unessential (U)	10,27±0,14	13,26±0,11	<0,01
E/U ratio	0,97±0,06	0,90±0,08	>0,05

The change from a mixed diet to intake of carbohydrates alone could worsen protein metabolism and cause development of protein deficiency. Such danger exists due to the limited protein reserve in the body and need for regular replenishment of amino acid outlay, particularly essential ones. Moreover, when there is a calorie deficiency, amino acids of tissues could be used for energy, rather than plastic purposes as a result of gluconeogenesis, which increases even more the shortage of these nutrients in the body.

Amino acid levels in blood plasma constitute an important indicator of adequacy of amino acids. Table 4 lists the levels of free amino acids in subjects' blood plasma before and after 5 days on a low-calorie carbohydrate diet. Venous blood amino acids were assayed using a Hitachi automatic analyzer, based on ion-exchange chromatography.

Analysis of the data in Table 4 leads us to mention, first of all, that most of the assayed amino acids remained within the normal range given in the latest edition of the BME [Great Medical Encyclopedia] (Vol 12) [6], before and after 5 days on emergency carbohydrate rations. Aspartic acid was an exception--its levels in blood were considerably lower than those listed in BME in all of the subjects, before and after using the emergency rations. In addition, there was a 164 and 138% increase in concentrations of isoleucine and histidine, respectively, after the 5th day of the study. Conversely, arginine content decreased, but negligibly (by 15%).

When evaluating protein metabolism, the greatest concern is usually referable to the decrease in blood amino acid content as an indicator of insufficient intake thereof with food and increased expenditure in the body. From this point of view, the data on overall amounts of blood plasma amino acids are indicative of the opposite tendency.

Overall essential amino acids increased by 19.6% and unessential by 29%. The ratio between them changed somewhat, due to relatively greater increase in essential amino acids.

Studies of levels of the different amino acids revealed that in 5 days lysine level dropped by 9.3%, glycine by 13%, threonine by 25%, arginine by 13%, proline by 12.4%, cystine by 6% and tyrosine by 3.4%, which was in the normal range given in BME. This decline in the amino acids listed is attributable to the absence of protein in the rations consumed on the 2d-5th days of the study. It should be stressed that the decrease in amino acid concentration was insignificant and within the range of usual levels.

Against the background of the mentioned cases of decrease in blood plasma amino acids due to the protein-free diet, the data on elevation of levels of several amino acids of blood plasma with development of semistarvation merit special consideration. Considering the data of several authors, this phenomenon can be interpreted primarily as utilization of amino acids from the reserve protein and structures for the purpose of gluconeogenesis [7]. Such gluconeogenesis develops in the case of total and partial starvation in order to supply the brain and other physiological systems with vitally needed amounts of glucose, when glycogen and other endogenous sources thereof are being depleted or already exhausted [7, 8].

Studies of a number of authors revealed that, for gluconeogenesis, alanine, glutamic and aspartic acids, tyrosin are used primarily, as well as threonine, valine, phenylalanine, histidine, arginine, serine and proline [8]. For use in such gluconeogenesis, the amino acids are "extracted" from cell structures, as a result of which the levels thereof in blood plasma could rise. This is apparently the explanation for the elevation of levels of more than half the above-mentioned amino acids demonstrated in the subjects. At the same time, the relatively high levels of blood plasma amino acids are indicative of absence of marked shortage thereof and protein deficiency [9].

Table 5 lists the results of assaying total nitrogen in 24-h urine before, during and after using carbohydrate rations. With change to the protein-free low-calorie diet, all subjects presented a decrease in total nitrogen excretion already on the first day. On the following days, the decrease in nitrogen excretion in 24-h urine continued, and after 5 days on the carbohydrate rations it reached a mean level of 8.60±0.23 g/day, versus

15.34±0.45 g/day on the eve of the tests. Thus, the body expended at least 53.75 g protein for gluconeogenesis on the 5th day (8.60×6.25). In all, over the 5-day period, loss of nitrogen in urine constituted a mean of 50.33± 0.53 g. On the protein-free diet, loss of nitrogen in feces, sweat and by other routes is not significant, according to FAO/WHO, constituting approximately 17 mg/kg body weight, or 1.19 g/day for a man weighing an average of 70 kg [10]. Consequently, loss of nitrogen via these routes should constitute an average of about 6 g in 5 days. Thus, overall loss of nitrogen in 5 days constituted 60 g in our subjects. There was a negative nitrogen balance each day. It is known that the human body contains about 1000 g nitrogen, and loss of 50% of this amount is considered fatal. The above estimates indicate that nitrogen loss by the subjects during the 5 days they spent on a low-calorie carbohydrate diet did not exceed 6%, which is indicative of only the initial stage of protein deficiency, which is not usually associated with dangerous clinical manifestations and is readily reversible upon returning to the usual diet.

Table 5. Total nitrogen excretion (grams) in 24-h urine before, during and after use of low-calory carbohydrate emergency rations

Subject	Usual diet, day		Low-calory carbohydrate diet, day							Recovery diet after intake of emergency rations, day		Usual diet on 5th day after intake of emergency rations
	1	2	1	2	3	1–3	4	5	1–5	1	2	
L-y	13.27	17,15	12,59	10,52	10,38	33,49	9,80	9,30	52,59	10,41	13,91	16.58
P-v	15,60	14,85	14,00	10,10	9,05	33,15	10,05	8,95	52,15	10,84	12,88	16.41
Kh-v	16,40	15,46	12,10	11,50	9,52	33,12	8,20	7,62	48,94	10,58	13,76	15.28
L-ch	15,31	17,14	14,04	10,11	8,50	32,65	8,69	8,13	49,47	12,20	14,73	15,10
V-ts	15,80	14,71	12,20	11,28	9,83	33,31	9,51	8,30	51,12	12,63	14,52	15,38
K-ev	13.5	13,95	11,94	9,28	8,90	30,12	9,86	8,82	48,80	10,10	12,88	15.37
K-ov	13,80	13,99	11,75	9,83	8,51	30,09	9,90	9,25	49,25	10,04	13,72	16,18

Indeed, as shown in Table 5, nitrogen excretion was quite satisfactory on the 3d day of the recovery period, and in some subjects it was close to the base level. This occurred on the first few days after our study, when the subjects were not on the usual diet, but one with fewer calories, less protein and fat. It should also be noted that nitrogen excretion in urine was above 37 mg/day/kg weight, the level observed when on a protein-free isocalorie diet during the period of minimal elimination of nitrogen [10].

Our studies warrant the conclusion that "survival" rations consisting of 300 g carbohydrates (sugar or caramel) can be deemed permissible, according to the set of parameters of nutritional status and the conclusion of the subjects themselves, for use for 5 days, let alone 3, as low-calorie emergency rations when there is limited expenditure of energy (3000-3200 kcal/day) and with fluid intake of up to 1 ℓ/day in a temperate climate. Of course, further studies are needed in hot and cold climates to determine the state of metabolism under these conditions and settle the question of desirability of including food supplements to carbohydrate rations to correct different elements of metabolism.

The results of these studies also lead us to conclude that the initial nutritional status is very important to "survival" in emergency situations. This compels us to consider optimum preflight nutrition as an important hygienic factor, not only to maintain inflight work capacity, but to safeguard health in cases of emergency landing on the ground or water.

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DYNAMICS OF LEFT VENTRICULAR SYSTOLIC PHASE STRUCTURE DURING LONG-TERM (140-185 DAYS) SPACEFLIGHTS

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[Article by A. P. Polyakova, A. D. Yegorov and I. V. Alferova]

> [English abstract from source] Kinetocardiographic studies of the left ventricular systolic time intervals at rest in spaceflights of 140, 175 and 185 days in duration revealed functional changes reflecting cardiovascular adaptation to weightlessness. The typical changes were: shortening of isometric contraction, decrease of the tension index, irregular decline of the ejection time, and a slight increase in the intrasystolic index. These changes in the systolic time intervals are indicative of an enhanced strength of cardiac contraction. This may in turn be associated with cephalad fluid shifts and reduced activity of the peripheral muscular heart.

[Text] Analysis of data in the literature indicates that certain changes occur in the phase structure of the cardiac cycle during spaceflights [1-4]. However, this has not yet been sufficiently investigated with regard to spaceflights lasting 3-6 months, and the available material has not been completely summarized or analyzed.

On the basis of current conceptions, there can be development of changes in intracardiac and systemic hemodynamics and extracardiac regulation during long-term weightlessness [5-7], which apparently also affects the phase structure of the cardiac cycle. Consequently, comprehensive studies of phase structure of the cardiac cycle are quite important to comprehension of mechanisms of adaptation of the cardiovascular system to function in weightlessness, as well as for ongoing evaluation of myocardial contractile function during long-term spaceflights.

Methods

To study the left ventricular systolic phase structure during long-term spaceflights, onboard Polynome-2M equipment was used to record the resting kinetocardiogram (KKG) and the data were transmitted to earth via telemetry channels. We used a piezoceramic sensor, the receiver part of which, in the form of a rubber capsule (4×6 cm in size) filled with paralon [typo for porolon?--foamed plastic], was placed in the region of the apex beat [8]. The KKG was interpreted by the method of L. B. Andreyev and N. B. Andreyeva [9] as modified by V. A. Degtyarev. We measured (in milliseconds) duration of the cardiac cycle (RR), electromechanical systole (EMS), mechanical systole (MS), phases of isometric contraction (IC) and ejection period (EP). Nominal mechanical systole and ejection period were determined using the formulas proposed by V. L. Karpman [10]: $MS = 0.144\ RR + 0.185$; $EP = 0.109\ RR + 0.159$. We also determined derivative parameters: myocardial tension index ($MTI = EP/EMS\ 100\%$), interphase coefficient ($IPC = IC/EP$), intrasystolic index ($ISI = EP/MS\ 100\%$) and ratio of actual duration of mechanical systole and ejection period to their nominal duration. The obtained primary data were submitted to statistical analysis by the method of variance analysis, and upon determination of the significance of effects, the mean parameters (for each month of flight) were compared to the preflight values (S method of multiple comparison [11]). For objective evaluation of the dynamics, we equated experimental data as a function of flight duration by the least squares method. The studies were conducted at rest on commanders (CDR) and flight engineers (FLE) who participated in 140- (CDR-2, FLE-2), 175- (CDR-3, FLE-3) and 185- (CDR-4, FLE-4) day flights.

Results and Discussion

Variance analysis revealed a statistically significant effect of study conditions and duration of flight on all of the parameters examined in all six cosmonauts ($P<0.05$). Further analysis of the obtained data enabled us to demonstrate both general patterns in the dynamics of inflight parameters and individual fluctuations. There was consistent reduction of the cardiac cycle in all cosmonauts as a function of flight duration. In four cosmonauts, the cardiac cycle progressively diminished over the entire duration of the flight, whereas in two cases this parameter increased somewhat after an initial decline. It was lower than the preflight duration with statistical significance in CDR-2, FLE-2 and CDR-4, whereas in CDR-3, FLE-3 and FLE-4 it usually coincided with preflight data, and even exceeded them in some tests.

Duration of the mechanical systole decreased somewhat in CDR-2 and FLE-3 as a function of flight duration, but virtually no specific direction of change was demonstrable in the other cosmonauts. The differences between inflight and preflight data were not statistically significant, although in most cases the duration of the mechanical systole was shorter than the mean preflight level. This was particularly evident on the example of the ratio of actual mechanical systole to nominal: this parameter was lower in the FLE-3, CDR-4 and FLE-4, not only than the mean preflight level, but minimal preflight value. The duration of phases of asynchronous contraction did not show statistically significant increase over the preflight level in three cosmonauts (FLE-2, CDR-3, CDR-4), and in the other three it did not differ from the preflight value or was even lower than the latter.

The duration of phase of isometric contraction was usually shorter, with statistical significance, than preflight values in 5 cosmonauts out of 6, and only in the CDR-4 was it virtually the same as preflight. In assessing the dynamics of two cosmonauts (CDR-2 and FLE-4), we found a tendency toward some decrease in duration of isometric contraction at the start of the flight and slight increase at the end. No definite dynamics were demonstrable in FLE-2 and CDR-4; an initial increase was followed by decrease in CDR-3 and FLE-3, while FLE-3 showed a second increase of this parameter by the end of the flight (Figure 1).

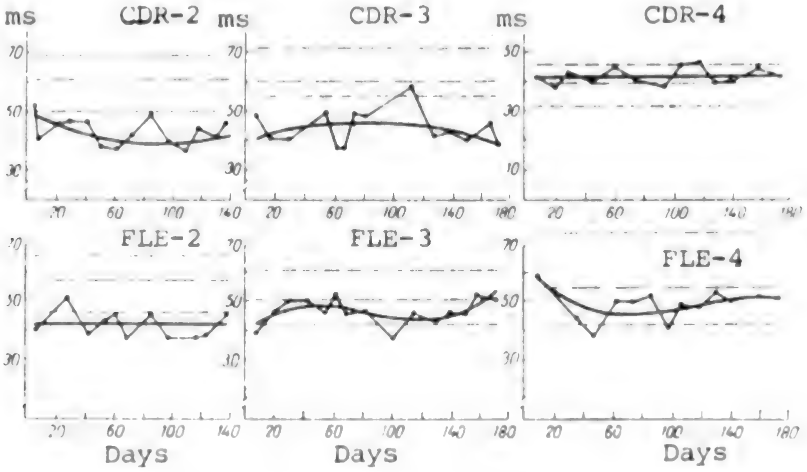

Figure 1. Dynamics of mean duration of isometric contraction of left ventricle in crews of Salyut-6--Soyuz orbital complex during flight, at rest.

Here and in Figures 2-4, the solid line refers to mean parameter on different days of flight (lines or smooth curves--smoothed data characterizing direction of inflight changes); dash line refers to range of fluctuation of parameter in the preflight period and dot-dash line shows mean preflight value of parameter

As compared to the mean preflight level, the ejection period was extended with statistical significance during the entire flight for FLE-2 and CDR-3 and for the first 2-3 months in CDR-2 and FLE-3. This parameter was lower, with statistical significance, than preflight values in CDR-4; it was above preflight levels in FLE-4 in the 1st and 6th months of flight, but lower in the 2d, 4th and 5th months. Studies of inflight dynamics revealed that the ejection period became shorter in three cosmonauts (CDR-2, FLE-3 and CDR-4) as a function of flight duration; no particular direction of change in this parameter was demonstrable in two cosmonauts (FLE-2 and FLE-4), while in CDR-3 the initial negligible increase was followed by decrease in the second half of the flight (Figure 2). The ratio of actual ejection period to nominal value was higher than the preflight level in three cosmonauts (CDR-2, FLE-2 and CDR-3), lower in two (CDR-4 and FLE-4) and showed negligible fluctuation in FLE-3.

Myocardial tension index had a tendency to increase in four cosmonauts (after an initial decrease in two of them) as a function of flight duration, whereas in CDR-2 and FLE-4 it showed no specific direction of inflight changes. The myocardial tension index, as well as interphase coefficient, were below the preflight levels in five cosmonauts and above only in CDR-4 (Figure 3).

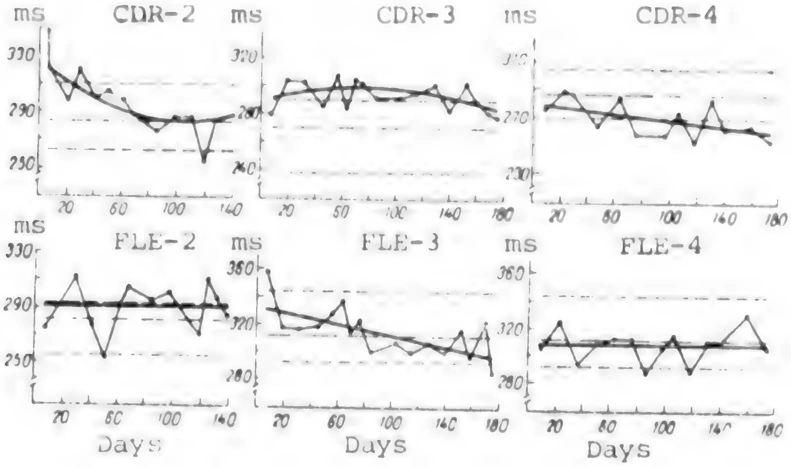

Figure 2. Dynamics of mean duration of left ventricular ejection period in crews of Salyut-6--Soyuz orbital complex during flight, at rest

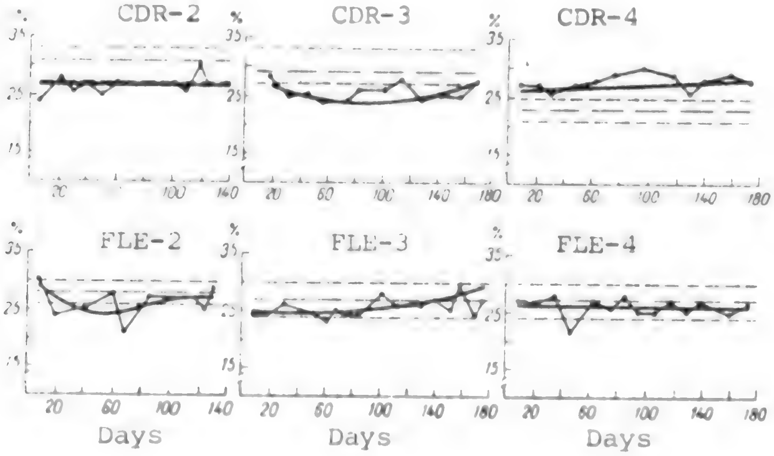

Figure 3. Dynamics of mean left ventricular myocardial tension index in crews of Salyut-6--Soyuz orbital complex during flight, at rest

The intrasystolic index was characterized by insignificant dynamics during the flights in all cosmonauts. We could merely detect a mild tendency toward increase of this parameter in CDR-2 throughout the flight and a mild tendency toward decrease in FLE-3. At the same time, the intrasystolic index usually exceeded the mean preflight level, and was below it only in CDR-4 (Figure 4).

Thus, we observed the following general changes in phase structure of the left ventricular systole in the course of 140-185-day flights: statistically significant shortening of phase of isometric contraction with concurrent appreciable reduction of myocardial tension index and interphase coefficient; inconsistent statistically significant increase in ejection period, mainly during the first months of flight (4 cosmonauts) with concurrent increase (by no more than 6-9%) in ratio of actual value of this parameter to nominal value;

some increase of intrasystolic index. The demonstrated changes in phase structure of the cardiac cycle during long-term flights are typical of the changes observed, according to the data of V. L. Karpman [12], with increase in strength of cardiac contraction (reduction of isometric contraction phase, myocardial tension index, etc.). The mechanism of this phenomenon in weightlessness is quite complex. It is believed that the shifting of blood in weightlessness, in a cranial direction, leads to increase in venous return and volumetric load on the heart [6, 7]. Increase of influx of blood and filling of ventricles, which leads to stretching of the myocardium, in accordance with Starling's law, increases the developed tension or amplitude of contraction due to increase in initial length of myocardial cells, i.e., it increases the force of cardiac contraction, which is associated with shortening of isometric contraction phase [10, 12]. The decrease in peripheral resistance, which was demonstrated [13] during long-term flights, may play some part in shortening the phase of isometric contraction. At the same time, the redistribution of blood and assumed (due to insufficient load on the muscle) decrease in activity of the peripheral muscular heart [14] probably increase systolic function of the heart and cause an increase in the role of active diastole in hemodynamics, which is manifested, in particular, by increase in duration of the rapid filling phase [4]. At the same time, it is known that increased duration of ventricular filling is involved in elevation of end diastolic pressure in the ventricle and decrease of difference between diastolic pressure in the aorta and ventricle which, according to V. L. Karpman [10], shortens the phase of isometric contraction.

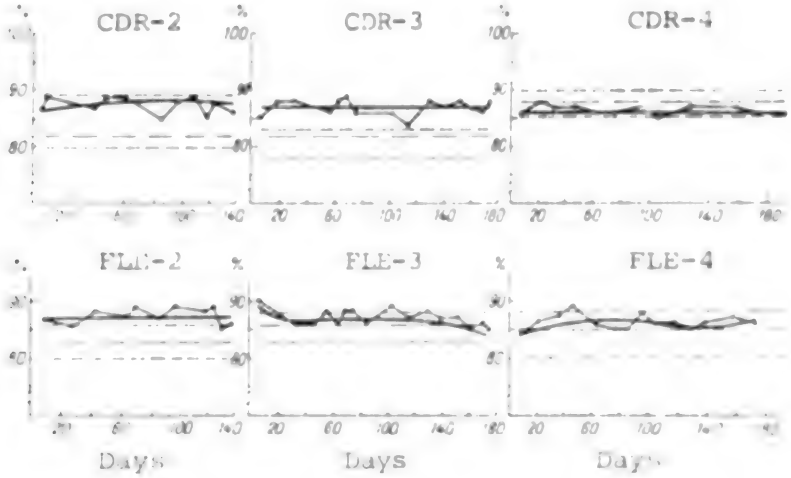

Figure 4. Dynamics of mean intrasystolic index of the left ventricle in crews of Salyut-6--Soyuz orbital complex during flight, at rest

The changes in phase of isometric contraction and ejection period demonstrated in flight also determine the dynamics of productive parameters. This is manifested by a decrease of the interphase coefficient and myocardial tension index (shorter time spent on preparing for ejection of blood from the heart), as well as moderate increase of the intrasystolic index (increased share of time spent for the heart to eject blood into the great vessels).

It is important to note that the changes in parameters of phase structure of the left ventricular systole, which are inherent in volumetric load on the heart, persist to some extent or other throughout the flight. However, as we have already mentioned, the severity of these changes may diminish toward the end of the flight in a number of cases (in the second half of the flight, ejection period diminished to the preflight level in FLE-3 and CDR-2).

Persistence of signs of increased force of cardiac contraction is consistent with data to the effect that redistribution in weightlessness of fluid, in a cranial direction (in spite of partial loss thereof during the flight) is present throughout long-term flights. This is indicated by the shift of the mass center in a cephalad direction found during the 84-day mission on Skylab programs [15], as well as decrease in volume of lower extremities [6, 7, 15], elevation of venous pressure in the jugular veins [16] and tendency toward retention of increased minute volume [6, 7, 17]. There is also an insufficient load on muscles during long-term flights and, consequently, there is a decrease in activity of the peripheral muscular heart.

It should be noted that signs of functional myocardial hypodynamia develop when conducting lower body negative pressure tests (during period of negative pressure). Changes are then observed, which are the opposite of those found during studies at rest during flights. These data are indicative of the reversible and functional nature of changes in phase structure of the cardiac cycle, which reflect the process of cardiac adaptation to different hemodynamic correlations, which are formed in weightlessness.

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UDC: 629.78:[612.16+616.171.1

SLOW WAVES OF CARDIAC RHYTHM IN HEALTHY MAN UNDER DIFFERENT CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 14 May 81) pp 30-32

[Article by A. N. Karpov and L. A. Zinov'yeva]

[English abstract from source] The slow waves of the cardiac rhythm were investigated at rest and under emotional and physical stress. In most test subjects emotional stress led to the generation of the first order slow waves of 0.04-0.09 cps, whereas exercises inhibited slow waves of the above frequency range. Heart rate increased in response to both emotional and physical stress. The slow wave responses can be used to evaluate the emotional status and to differentiate emotional and physical stress.

[Text] Changes in periodic components of cardiac rhythm, interest in which has heightened because of the popularity of autocorrelation and spectral analysis [1, 2], have been used in recent times as objective indicators of functional working tension [3], fatigue [4], emotional state [5] and various pathological processes [6, 7].

At the same time, the mechanisms of formation and change in slow waves of heart rhythm have not yet been fully identified [8], whereas there is no agreement on the question of frequency range of these waves [2, 3, 9, 10].

Our objective here was to study the stability of frequency characteristics of first order slow waves, as well as demonstrate individual distinctions and general patterns of changes therein, depending on the functional state of subjects.

Methods

A total of 17 essentially healthy men, 28 to 53 years of age, participated in the study; they consisted of transport aviation flight personnel. The test procedure consisted of successively performing the "black and red table" test and, after a 10-min break, a cancellation test and two-step step test at the rate of 60 steps/min.

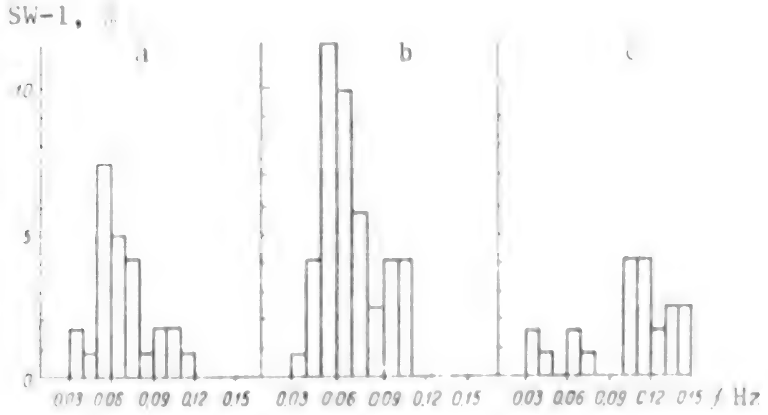
There was a practice "black and red table" test for adaptation purposes, as well as to produce a certain level of mobilization in the subjects before the actual test. The cancellation test, which was to be done in a limited time, simulated emotional tension [11], development of which was caused by the increased motivation obtained by including our study in the program of the educational and training process. The step test developed a state of moderate physical tension, whereas the subject's state during the break prior to the cancellation test was considered as operative rest. We conducted 5 to 8 tests with each subject within 1 month. In the course thereof, we recorded the EKG and pneumograms, starting in the 6th min of the rest period and 6th min of the cancellation and step tests, i.e., after a stable state had been reached [12].

Series of R-R intervals were obtained on the EKG, which lasted 80 s each, were submitted to processing by methods of autocorrelation and spectral analysis on an M-6000 computer. The pneumogram was used to differentiate between respiratory arrhythmia and first order slow waves (SW-1) when the latter were at a high frequency. According to the data of different authors, the SW-1 frequency range constituted 0.033-0.125 Hz [2-3].

In the course of the study we made 121 tests and obtained 363 spectral density charts, from which we determined whether SW-1 were present on the subjects' rhythmograms.

Results and Discussion

The Figure illustrates the results of our studies. It shows the number of rhythmograms with SW-1 (as a percentage of number of cases; n = 121 for each of three experimental conditions) and distribution of SW-1 according to frequency, depending on test conditions.



Number of SW-1 on rhythmograms of subjects (% of cases) and their distribution according to frequency, as related to test conditions

a) operative rest b) cancellation test c) step test

The figure shows that SW-1 are demonstrable in the subjects whatever their state, although the frequency varied. A change in emotional state of a subject due to performance of the cancellation test led to considerable increase in number of SW-1. Use of the sign criterion to evaluate the entire sample, we obtained a high reliability of difference ($P<0.01$). However, among the subjects, there was a group of 4 men in whom opposite reactions prevailed ($P<0.05$). This can be satisfactorily explained only by development of different types of emotional reactions in the subjects: asthenic (1st group and as a general tendency in the entire sample) and sthenic (2d group).

The results of evaluating overall productivity (productivity with consideration of mistakes) in the cancellation test can serve as indirect confirmation of the link between the sthenic emotional reaction and depression of SW-1. In the absence of SW-1 on rhythmograms ($n = 61$), overall productivity was reliably greater than in the presence thereof ($n = 60$, $P<0.01$ according to the F criterion).

Moreover, we see that physical tension, which was associated with intensification of sympathetic influences, elicited depression of SW-1, and this applied mainly to waves of 0.04-0.09 Hz, while the number of faster waves increased.

While the mean frequency of SW-1 at rest and during the cancellation test constituted 0.070 and 0.071 Hz, respectively, during physical work there was prevalence of waves with a mean frequency of 0.108 Hz, which is quite different from the first two ($P<0.001$ according to t criterion).

With regard to the SW reaction to different loads, we must also mention the changes in heart rate (HR). The latter were insignificant in most cases (average of 2.8/min), but increased reliably ($P<0.01$ according to sign criterion) during the cancellation test. Pilots A. and Sh. were the only exceptions: their HR decreased. In all cases, the step test elicited a more significant increase of HR.

Thus, we see that, in most subjects, emotional reactions associated with intensive mental activity elicited changes in SW-1 that were the opposite of the changes during physical work, whereas HR could not be an informative indicator for differentiation between emotional and physical tension.

Expressly these properties of SW-1 are of the greatest interest and lead us to expect that the reactions of these waves will find a definite place among objective methods of determining emotional states.

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SYNCHRONIZATION OF CARDIOVASCULAR ACCIDENTS WITH PHYSICAL CLOCKS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 8 Sep 81) pp 32-34

[Article by R. M. Arslanova, V. N. Benevolenskiy, N. G. Ptitsyna and K. A. Trukhanov]

[English abstract from source] Investigations were carried out to correlate the frequency of cardiovascular catastrophes (daily mortality rate of patients with ischemic heart disease), heliogeomagnetic activity (solar radiation in the wave band 10.7 cm, H, D and Z components of the geomagnetic field), synchronization and desynchronization of circaseptidian rhythms, and total number of cardiovascular catastrophes in different seasons. The raw data sets were treated with due account of the discrete pattern of random sequences and noise in the medical data set, finite analysis interval and informativity of the derivatives of the parameters used. The occurrence of cardiovascular catastrophes showed circaseptidian rhythms whose level depended on the above three factors. The results obtained are discussed with respect to possible synchronization and desynchronization of endogenous biorhythms by time cues, relating them to the mechanism of human adaptation to the environment.

[Text] In current biomedical research, considerable attention is given to theoretical and experimental examination of the role of various fluctuations of external physical factors in synchronizing endogenous biorhythms. Numerous studies [1-4] have demonstrated, in particular, that fluctuations of meteorological and geophysical conditions with a period of $T \approx 1$ day could serve as clocks for circadian biorhythms. Concordance of various circadian physical and biological rhythms is instrumental in normal function of the organism, while mismatch thereof leads to signs of desynchronosis and, consequently, functional disturbances in different systems and diminished adaptation capabilities.

Our purpose here was to study this matter as it relates to fluctuations of exogenous factors with a period exceeding 1 day.

Methods

We used components H, D and Z of the geomagnetic field, and flux of solar radiation at a wavelength of 10.7 cm--F, which characterize solar and geomagnetic activity, as physical clocks in this case. The biological parameter studied was the incidence of cardiovascular accidents, N (daily mortality due to ischemic heart disease in several parts of Moscow in 1969) [5].

The object of our study (in this case, the patient) was considered under actual living conditions. He is exposed to exogenous physical factors, which represent disturbance vector $X_q(k)$. The object's reaction is characterized by condition vector $N(k)$, an element of which is the daily intensity of cardiovascular accidents. Vector function $Y_p(k)$ characterizes noise at the output of the object, due to lack of correlation with input source disturbances: psychological stressors, functional distinctions of the body, etc. Operator g describes the law, according to which a set of input disturbances is matched to a set of medical parameters, and characterizes the channel that perceives information about changes in parameters of the tested exogenous physical factors.

Thus, the mathematical model of the effects amounts to the following:

$$N(k) = g[X_q(k)] - Y_p(k)$$

Proceeding from the assumption that there is a link only for some periodic components of heliogeomagnetic and medical parameters, we chose the spectral method as being the most informative to process base information. Evaluation of the link between periodic components of variables was made by means of the coherence function, which improves the accuracy of measurements as a result of elimination of structural distinctions of autospectra of the measured parameters. In addition, it was assumed that it was not the absolute magnitude of heliogeomagnetic disturbances, but their time derivatives that had the strongest effect on the body, due to the static nature of its defense and compensatory mechanisms. For this reason, we first analyzed the first differences in sequences, that had been previously processed by means of a filter [6].

Spectral analysis was performed in the Walsh basis [7]. To eliminate the effects of low-frequency components, the initial run consisting of 512 readings formed by synthesis of partially overlapping intervals was divided into 8 equal segments of 64 days each. For each of these 8 segments, we calculated estimates of the sample spectrum of power, which were then averaged according to recurrence frequency. We then averaged the sample spectrum according to adjacent recurrence frequencies grouped by the one-third octave principle. This approach enabled us to reduce the number of analyzed spectral components by eliminating superfluous details about the spectrum and the magnitude of variance error by widening the analysis band.

Results and Discussion

We demonstrated pronounced components in the range of fluctuations with periods of T = (5-7) days on the obtained power spectra of cardiovascular accidents and daily differences in heliogeomagnetic parameters. In this range, the true values of coherence functions fall into intervals [0.57, 0.79] for $\kappa_{N,\Delta H}$ and $\kappa_{N,\Delta D}$, and [0.68 and 0.88] for $\kappa_{N,\Delta Z}$ and $\kappa_{N,\Delta F}$.

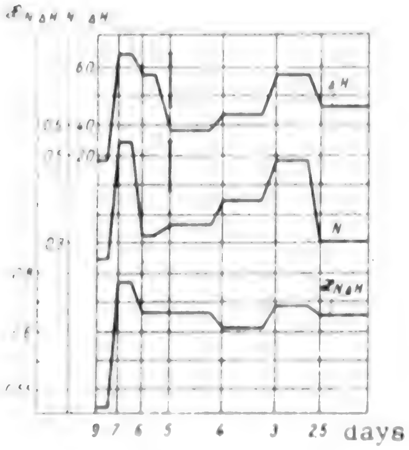

Figure 1.
Estimation of power spectra of daily differences in horizontal component of geomagnetic field ΔH, incidence of cardiovascular accidents N and their coherence functions $\kappa_{N\Delta H}$, calculated for the March-November interval

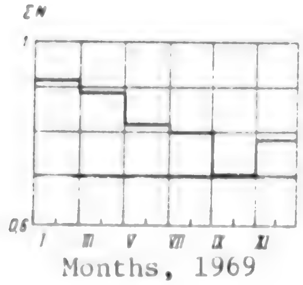

Figure 2.
Dynamics of relative number of cardiovascular accidents (ΣN) calculated for each of the current 2-month intervals

To illustrate the results, estimates of power spectra of differences between days in horizontal component of geomagnetic field ΔH, incidence of cardiovascular accidents N and their coherence functions $\kappa_{N,\Delta H}$ are shown on a logarithmic scale in Figure 1. The vertical segments mark 95% confidence intervals for spectrum components corresponding to fluctuations with a period of T = 5-7 days.

For a more detailed analysis, the estimates of power spectra N, ΔF, ΔH, ΔD and ΔZ, which were calculated for each of the 64-day intervals, were compared to the annual dynamics of cardiovascular accidents illustrated in Figure 2 and to the mean monthly values of indexes of K_p, A_p D_{st} variation and Wolf numbers reflecting heliogeomagnetic activity in the corresponding periods.

Figures 3 and 4 illustrate on a logarithmic scale estimates of power spectra obtained for intervals corresponding to minimum (September-October) and maximum incidence of cardiovascular accidents and analogous trends of heliogeomagnetic activity. In the fluctuation range with periods of T = (5-7) days, we should mention the marked synchronization of dynamics of power spectra N, ΔF, ΔH, ΔD and ΔZ (Figure 3) and desynchronization of quasi-weekly rhythms of mortality and heliogeomagnetic parameters (Figure 4). Maximum power of N in both cases is in the range of T = (5-7) days; however, in Figure 4 it is marked minimally, in spite of the higher mortality rate in Januar and February. The values of N shown in Figure 2, between the minimum and maximum, are characterized by an intermediate degree of mismatching of spectral structures of heliogeomagnetic parameters.

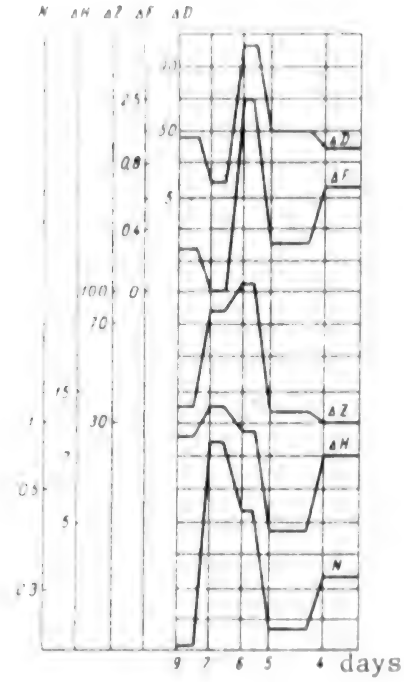

Figure 3.
Estimate of power spectra of daily differences in solar activity expressed by solar radiation at wave of 10.7 cm (ΔF), component of geomagnetic field (ΔN, ΔD and ΔZ), incidence of cardiovascular accidents (N), calculated for September-October interval

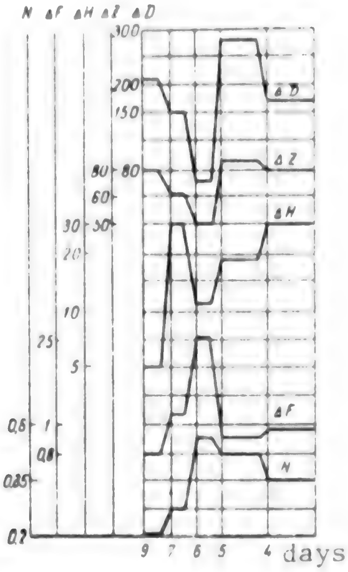

Figure 4.
Estimate of power spectra of daily differences in solar activity expressed by solar radiation at wave of 10.7 cm(ΔF), component of geomagnetic field (ΔH, ΔD and ΔZ), incidence of cardiovascular accidents (N), calculated for January-February interval

Thus, our findings indicate that not only circadian, but quasiweekly biorhythms interact with the rhythms of geomagnetic parameters, as a result of which there is synchronization or desynchronization of the body's rhythms with those of exogenous physical factors. Apparently, the situation when the period structures of quasiweekly physical clocks are strictly synchronized with one another and quasiweekly rhythms of the organism are best for the latter; desynchronization thereof intensifies adaptation mechanisms and, in a weakened organism, could lead to serious functional and structural disturbances. The latter could occur during periods of increased solar activity and, apparently, drastic increase in the natural electromagnetic background due to fields of commercial origin.

Analysis of our data confirms once more that the basic property of natural processes (rhythmicity) is very closely related to the mechanism of adaptation of the organic world to the inorganic environment.

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REGULATION OF CEREBRAL CIRCULATION IN ERECT POSITION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 29 Jun 81) pp 35-40

[Article by V. S. Shubin, V. L. Anzimirov, Ya. K. Gasanov and V. N. Korniyenko]

[English abstract from source] The functional mechanisms responsible for orthostatic tolerance of cerebral circulation in the normal man and in ambulatory and bedridden neurosurgical patients were investigated, using the following methods: cerebral serial angiography, measurement of cerebral blood flow by means of xenon-133 clearance, measurement of brain perfusion pressure, ventricular pressure, acid-base equilibrium in the blood flowing in and out of the brain, determination of cardiac output and stroke volume, electroencephalography, and rheography of cerebral and peripheral vessels. In the normal men and patients with compensated neurosurgical pathologies, the transfer into the head-up position induced small changes in the systemic and cerebral regional circulation. This was associated with complex reactions of the vascular system triggered by the receptors of the sinocarotid area. The normal response of the vascular system to the orthostatic load involved dilatation of cerebral and constriction of peripheral arteries, tachycardia, increased central venous pressure, moderate decrease of brain perfusion pressure and intraventricular pressure. In vascular pathological reactions constriction of peripheral arteries and veins was disturbed; cardiac output and stroke volume, cerebral blood flow velocity, central venous and intraventricular pressures were decreased.

[Text] It is known that in most quadrupeds a prolonged stay in erect position causes cerebral anemia, which sometimes leads to death. In the course of changing from horizontal to vertical position, man developed neurogenic defense mechanisms for regulation of cerebral circulation, which cause redistribution of blood when the position of the body changes. Baroreceptors, which have an inhibitory effect on vasomotor neurons of the medulla oblongata, play a leading role in expression of these mechanisms. Attenuation of this influence due to a pressure drop in the carotid sinus activates the sympathetic nervous system and leads to development of the pressor sinocarotid reflex [1], with which one observes constriction of veins [2], faster heart rate [3], increase in minute volume [4] and blood flow in pial arteries [5, 6], in addition to generalized constriction of resistive vessels.

Rheoencephalography was used to demonstrate a significant decrease in pulsed filling of cerebral vessels during orthostatic tests on patients with arterial hypotension [7, 8] and cerebrovascular pathology, whereas this parameter does not usually change, or else it rises in healthy subjects. Mechanisms of myogenic regulation of vascular tonus play an important part in providing for orthostatic stability of the circulatory system [9].

In view of the fact that most of the cited data were obtained in experiments with animals, our objective here was to pursue a combined study of changes in the main parameters of systemic and cerebral hemodynamics of man using the orthostatic test.

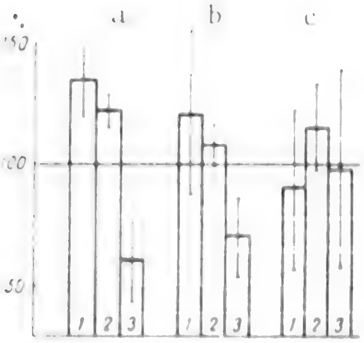

Figure 1.
Changes in rheographic parameters of cerebral and peripheral circulation in athletes (a) and patients of the first (b) and second (c) groups during orthostatic test. Y-axis, scale of changes in parameters (% of initial background).
1)CBF 2) HR 3) PBF

Methods

These studies involved the participation of 28 athletes and 38 neurosurgical patients 22 to 45 years of age, with tumors and vascular diseases of the brain without elevation of intracranial pressure and without signs of occlusion of the cerebrospinal fluid tracts. All of the patients were divided into two groups: the first consisted of ambulatory patients with compensated diseases and the second of patients who had been bedridden for a long time.

We conducted the following studies to characterize circulation: catheterization serial cerebral angiography (carotid and vertebral) in horizontal and vertical positions. We performed catheterization venography of the internal jugular vein and spinal venous plexus (contrast medium injected in distal parts of the sigmoid sinus) on 27 patients under the same conditions. We prolonged the angiogram films to 15-30 s in order to trace all phases of blood flow. Cerebral circulation time in different parts of the vascular bed was calculated from the angiographic data.

The ^{133}Xe clearance method was used to measure cerebral volumetric blood flow; Xe was injected in the internal carotid. This test was performed on 12 patients. The collimators were placed over the temporal and parietal lobes, adhering strictly to the same geometry of calculation.

Perfusion pressure of the brain was determined from the difference between arterial pressure in the internal carotid and venous pressure in the bulb of the internal jugular vein or vertebral venous plexus (according to intraosseous pressure in the bodies of the 3d-4th cervical vertebrae). The zero point was set on the level of the external auditory meatus. This test was performed on 18 patients. Cerebrospinal fluid pressure was measured in one of the lateral cerebral ventricles in 22 patients. Mingograph-81 and Polygraph RM-150 equipment was used to record pressures, as well as electrocardiograms, electroencephalograms (EEG), frontomastoid rheoencephalograms and rheograms of the forearms. We used a 4-channel rheographic attachment at an operating frequency of 150 kHz. To interpret the rheographic parameters, we estimated amplitude parameters (A_x, in ohms), rheographic indicators of cerebral blood flow (CBF) and peripheral blood flow (PBF), which were the product of A_x multiplied by heart rate (RR) (in ohms/min).

Cardiac output was calculated with the formula of Bremser-Ranke, using tacho-oscillography to find the initial parameters [3].

Before the angiographic examination, we took samples of blood flowing to and from the brain to determine the gas composition and acid-base state. We used a micromethod with the Astrup unit.

The following parameters were determined to characterize cerebral circulation and some metabolic parameters of the brain: stroke and minute volume (SV and MV), perfusion pressure of the brain, cerebral volumetric blood flow, cerebral blood flow time, oxygen uptake by the brain and resistance of its vessels. All of the digital data were submitted to statistical processing on a Nairi-2 computer.

Results and Discussion

The rheographic studies conducted on the 28 athletes revealed that there was marked, statistically reliable increase in CBF, HR and decrease in PBF during the orthostatic test. There was decline of cerebrovascular tonus and increase in tonus of peripheral vessels. Tests on the first group of patients revealed the same patterns; however, there were less marked changes in rheographic parameters and HR.

In the second group of subjects, the change to orthostatic position was associated with decline of CBF and increase in HR, without changes in the initially high PBF. Tonus of cerebral vessels diminished, whereas the low tonus of peripheral vessels remained unchanged. Comparative data on changes in rheographic indicators of cerebral and peripheral circulation and HR of healthy subjects and patients are illustrated in Figure 1.

In the second group of patients, the background EEG tracings showed irregularity of α rhythm, some slowing of bioelectric activity of the brain with prevalence of low-amplitude δ waves, with retention of α and β waves. During the orthostatic test, there was an appreciable increase in slow potentials, with signs of mild stimulation of stem structures.

In the second group of patients, the general cerebral changes in bioelectric activity were more marked, and they increased appreciably with the orthostatic test, as manifested by prevalence of diffuse slow activity, not infrequent paroxysmal bursts of θ and δ waves, which were indicative of more significant stimulation of stem structures of the brain.

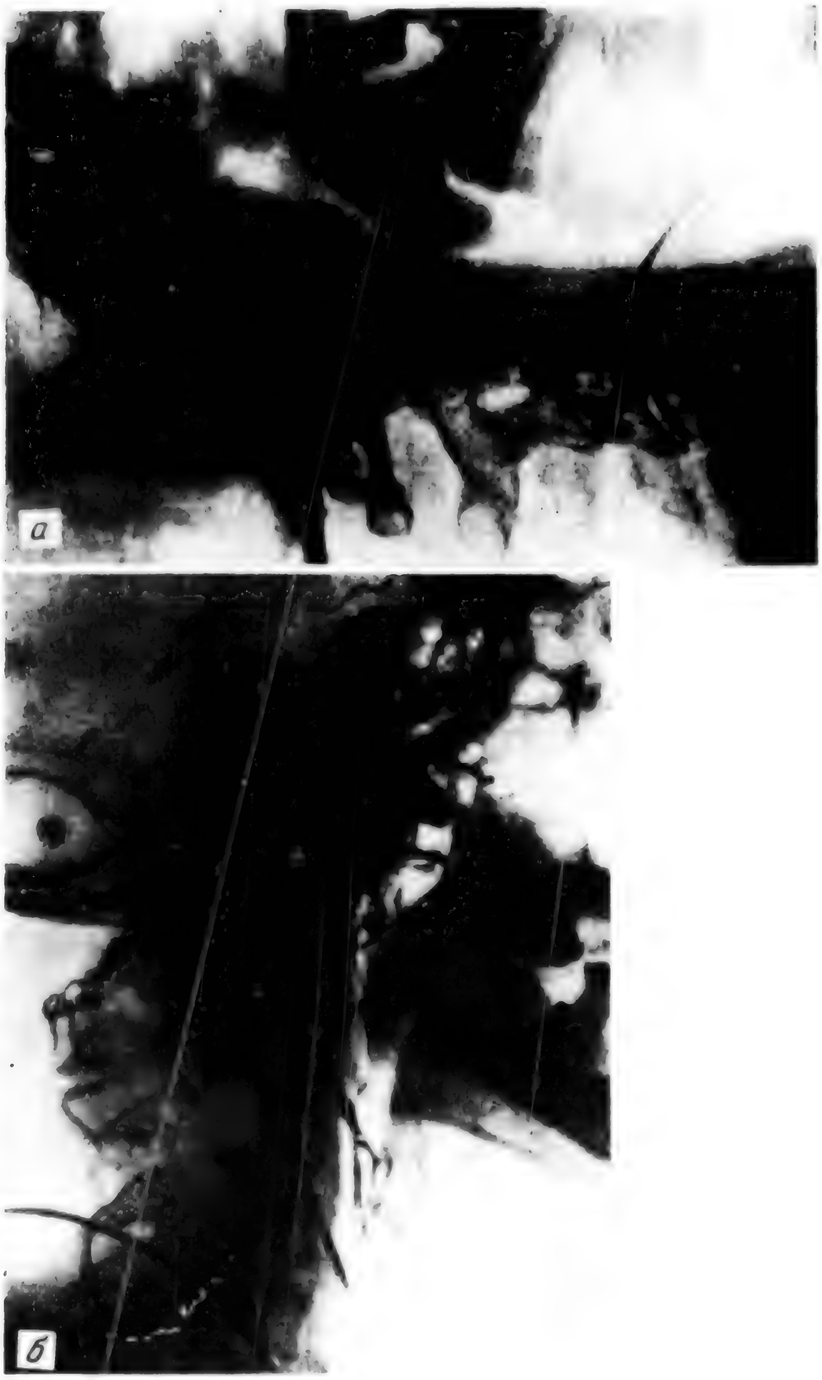

Figure 2. Sinusography and jugulograph in supine (*a*) and seated (б) positions for a patient in the first group

a) efflux of blood from carnium in internal jugular vein

б) efflux through vertebral venous plexus

Changes in main parameters of systemic and cerebral hemodynamics during orthostatic test on patients referable to first and second groups

Parameter	Group of patients			
	1		2	
	background	orthostatic test	background	orthostatic test
Blood flow time in cerebral arteries, s	2,75±0,68	5,1±0,98	3,24±0,91	7.22±2.16
	$P<0,05$		$P<0,05$	
Total cerebral blood flow time, s	7,35±1,31	11,4±1,61	8,43±1,82	13.2±3.91
	$P<0,05$		$P<0,05$	
Cerebral perfusion pressure, mm Hg	93,6±1,5	73,6±1,2	109,5±0,9	92,7±5,7
	$P<0,001$		$P<0,02$	
Ventricular pressure, mm Hg	16,80±1,96	12,17±1,66	18,7±5,53	2,46±4,16
	$P>0,05$		$P<0,05$	
Regional cerebral blood flow, mℓ/100 g/min	48,59±0,73	50,31±0,71	46,07±1,61	38,24±2,07
	$P>0,05$		$P<0.02$	
MV, mℓ/min	5531±1365	5978±1595	6335±1588	5569±1127
	$P>0,05$		$P>0,05$	
SV, mℓ/min	61,57±19,2	64,31±17,6	69±9	49,6±8,4
	$P>0,05$		$P<0,02$	
HR, per min	71,8±5,76	76,8±7,79	90,8±12,07	112,6±15,8
	$P>0,05$		$P<0,05$	
Mean pressure in bulb of internal jugular vein, mm Hg	5,±41,4	11,4±2,6	7,5±1,8	3,3±1,1
	$P<0,05$		$P<0,05$	
Mean pressure in internal carotid artery, mm Hg	99,0±6,9	85,0±4,5	117,0±8,1	96,0±7,2
	$P>0,05$		$P<0,05$	

The results of studies of the main hemodynamic parameters of patients in the first and second groups (see Table) revealed that cerebral blood flow time increased reliably in erect position, mainly due to its arterial phase, whereas perfusion pressure of the brain and pressure in the internal carotid dropped, which is indicative of dilatation of cerebral vessels. We demonstrated a convincing difference between changes in venous pressure in the first and second groups of patients: while the orthostatic test led to appreciable elevation of pressure in the bulb of the internal jugular in the first group, marked drop of venous pressure was observed in the second. The rise of venous pressure in patients with the normal type of orthostatic reaction was apparently due to reflex increase in venous tonus; this reaction was not manifested in decompensated patients. In erect position, compensated patients presented a moderate decline of ventricular pressure, which was probably due to redistribution of cerebrospinal fluid in the subarachnoid space of the spinal cord, whereas decompensated patients presented a drastic drop of ventricular pressure (from 18.7±5.5 to 2.46±4.16 mm Hg). Normal function of mechanisms of compensation of cerebral blood flow in orthostatic position in the first group of patients was the reason for absence of appreciable changes in regional cerebral blood flow, which diminished appreciably in patients of the second group. The

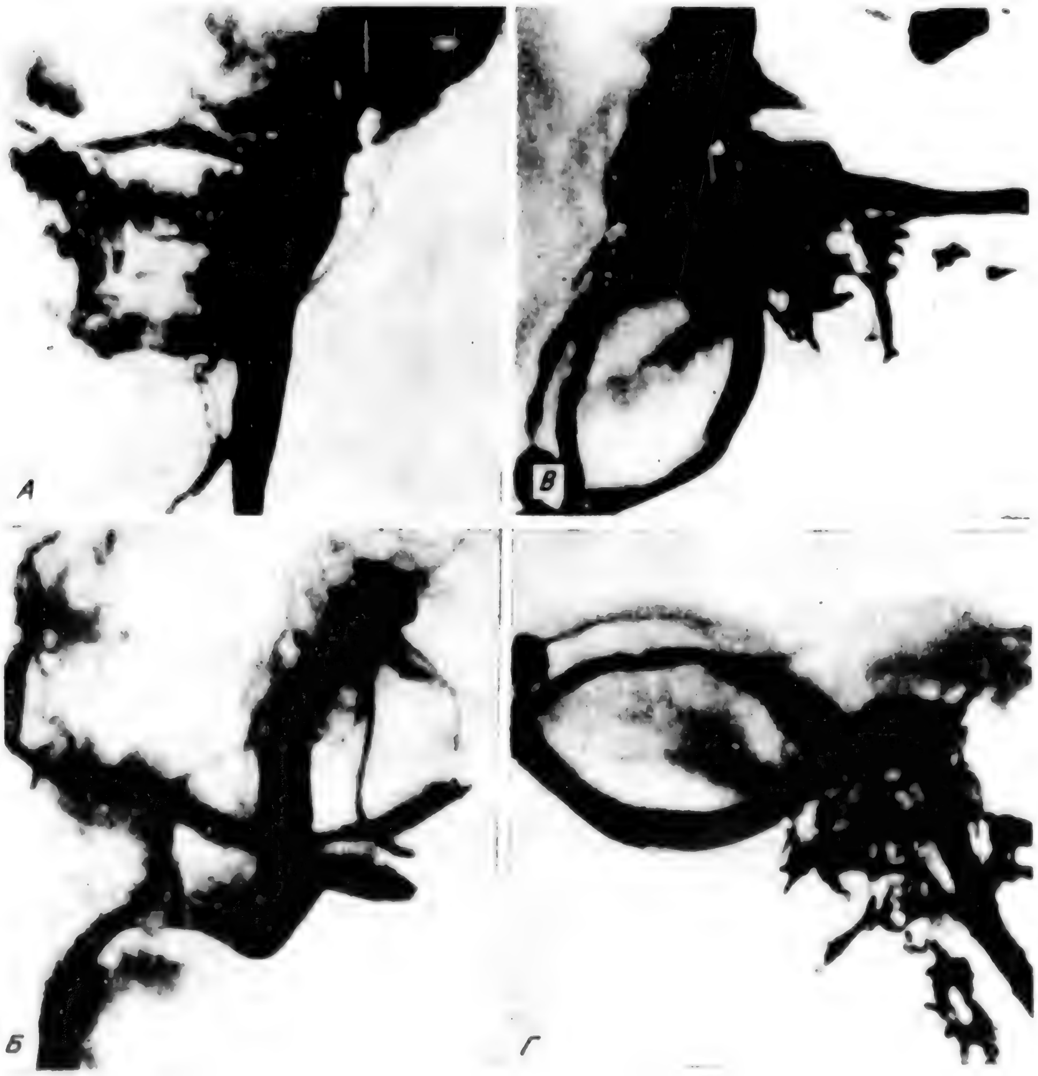

Figure 3. Sinusography and jugulography in supine (A, B) and seated (Б, Г) positions in a patient from second group in antero-posterior (A, Б) and lateral (B, Г) projections. Efflux of blood from cranial cavity proceeds through jugular vein and, in part, vertebral venous plexus, in both horizontal and vertical positions

change to vertical position of patients in the first group did not affect SV and increased only negligibly the degree of increase in HR and MV. At the same time, patients in the second group presented marked, statistically reliable decrease of SV, which was associated with tachycardia, for which reason MV decline was insignificant.

In order to determine the main routes of venous efflux from the cranial cavity, we performed jugulography on 18 patients from the first group and 10 from the second, by injecting contrast medium into the distal parts of the sigmoid sinus. Analysis of the obtained data revealed that, with the patients of the first group in supine position, efflux from the cranial cavity occurred chiefly over the internal jugular veins and, to an insignificant extent, the venous plexus of the vertebral canal. In seated position, the jugular veins were virtually closed, and efflux of venous blood occurred through the vertebral venous plexus and cervical veins around it (Figure 2). In the second group of patients, efflux of blood from the cranium occurred to an equal extent over both routes in both seated and supine positions (Figure 3).

As a result of our studies, it was determined that the change to erect position of healthy subjects and patients in the first group caused development of a number of compensatory reactions aimed at stabilizing systemic hemodynamics, in the form of generalized constriction of peripheral arteries and veins, and moderate tachycardia. In spite of the slight drop of cerebral perfusion pressure, the vasodilatation of cerebral vessels provided for adequate cerebral blood flow and was not associated with disturbances in bioelectric activity of the brain. The demonstrated difference in direction of venous efflux in horizontal and vertical positions is apparently a compensatory reaction by the venous system, which occurs due to constriction of internal jugular veins and direction of venous efflux to the spinal cord, which prevents drastic displacement of cerebrospinal fluid from cerebral ventricles into the spinal part of the system of cerebrospinal fluid.

The second group of patients presented gradual adaptation of the sinocarotid reflex [10-13] due to prolonged stabilization of pressure in the carotid sinus. Similar attenuation of the sinocarotid reflex can develop as a result of impairment of sympathetic innervation of the carotid arteries [14, 15] or cerebrovascular pathology.

There were no constrictor reactions of peripheral arteries and veins, or else they were attenuated, causing decrease in SV, in patients with impaired excitability of the sinocarotid system. There was mild dilatation of cerebral vessels and, in spite of the fact that cerebral perfusion pressure did not drop below the critical level [16], we observed a decrease in volumetric velocity of cerebral blood flow and appearance of dominant bilateral slow activity on the EEG, which were indicative of signs of cerebral hypoxia. The cerebral hemodynamic disturbances are aggravated by the drastic drop of ventricular pressure, due to impairment of mechanisms involved in constriction of internal jugular veins.

Since we failed to demonstrate appreciable differences in the nature of pathological vascular reactions in orthostatic position in decompensated patients with different levels of brain lesions (stem, diencephalic region, basilar and convexital cortex), one would think that hypodynamia, which causes adaptation of the sinocarotid reflex, was the chief cause of impairment of orthostatic stability.

At the present time, conditioning on an orthostatic table with use of anti-G suits, is included in the set of rehabilitation measures for patients with orthostatic instability [17]. We can also expect a beneficial therapeutic response to pharmacological activation of adrenergic systems.

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UDC: 612.014.477-053.85

ENDURANCE OF $+G_z$ G FORCES BY MIDDLE-AGED PEOPLE BEFORE AND AFTER 7-DAY IMMERSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 10 Apr 81) pp 40-43

[Article by A. R. Kotovskaya, I. F. Vil'-Vil'yams, V. I. Zborovskaya, V. G. Andreyeva, O. L. Golovkina, T.N. Krupina, Kh. Kh. Yarullin and N. P. Artamonova]

[English abstract from source] Before and after 7-day immersion 6 healthy male test subjects, aged 41 to 49, were exposed to $+3\ G_z$ for 60 sec in a centrifuge with an arm of 7.25 m. The runs were repeated 12 times. The test subjects well tolerated the exposure before and after immersion. However, after immersion the physiological systems functioned in a more stressful manner than prior to immersion. This can be attributed to the deconditioning caused by simulated weightlessness. The comparison of the experimental findings with the literature data gives evidence that the pattern and level of physiological changes induced by an exposure to $+3\ G_z$ for 60 sec in the test subjects, aged 41 to 49, do not differ significantly from those in younger (aged 23 to 36) people.

[Text] Development of cosmonautics is opening up the prospect of having highly qualified specialists over 40 years of age participate in future space missions. The data in the literature concerning the effect of age on endurance of accelerations are contradictory. Some authors report a decrease in endurance of $+G_z$ in individuals over 40 years of age [1], while others do not believe this is so [2].

After simulating the effects of weightlessness by means of bed rest lasting 10.5 days, there was a decrease in resistance of subjects 46-55 years of age to G forces of $+3\ G_z$; however, this decline was less marked than at the age of 35-45 years [3].

There is no information in the literature concerning resistance of older subjects to $+G_z$ accelerations after simulation of weightlessness by means of immersion. It is known that immersion simulates better than hypokinesia the changes referable to the cardiovascular system, skeletomuscular system and fluid-electrolyte balance in weightlessness [4, 5].

Our objective here was to study the physiological reactions of older subjects (41-49 years) to longitudinal, head-pelvis G forces after simulating the effects of weightlessness by means of immersion.

Methods

We conducted 12 tests on a centrifuge with a 7.25-m arm with 6 healthy men 41-49 years of age, who had no experience in flight work. The subjects were exposed to $+3\ G_z$ for 60 s, with a build-up gradient of 0.2 G/s before and after horizontal "dry" immersion up to the neck [7]. Immersion lasted 7 days. Water temperature in immersion tank was neutral for man (33.5±0.5°C) and kept at a constant level by means of a heat-regulating instrument.

The muscles of the prelum abdominale and lower extremities were kept tense in order to enhance endurance of accelerations during acceleration of the centrifuge and on the $+G_z$ plateau.

In all of the tests, during exposure to accelerations we recorded the EKG in the Neba leads with subsequent calculation of heart rate (HR), arterial pressure (AP) in the brachial region according to Korotkov sounds, systolic AP in earlobe vessels by the photoplethysmographic method, pneumogram, electromyogram (EMG) of the right femoral quadriceps, soleus and tibia of the right leg.

Before and after rotation on the centrifuge (after 40-50 min), we recorded the thoracic rheogram using an RPG2-02 tetrapolar rheograph, in order to estimate stroke (SV) volume and cardiac output (CO) by the method described in [8]. Total peripheral resistance (TPR) was determined using the formula of Poiseuille.

Determination was made of parameters of biomechanics of respiration by the method of pneumotachography and gas exchange according to Douglas-Haldane before and immediately after stopping the centrifuge for 5 min. We calculated respiration rate (f), tidal (V_T) and minute (V) volumes, as well as oxygen uptake (VO_2).

Gas exchange data are expressed in the STPD system and parameters of ventilation and biomechanics of respiration in the BTPS system.

All of the data were submitted to processing by the Student method of variational statistics. Differences were considered reliable at $P<0.05$.

Results and Discussion

Before immersion all of the subjects endured well the planned mode of exposure to accelerations. There were no disturbances referable to vision and cardiac rhythm. We observed sinus tachycardia (up to 128/min) and moderate tachypnea. AP level in earlobe vessels constituted a mean of 106 mm Hg and did not differ appreciably from base values. Systolic and diastolic AP in the arm [shoulder] region rose. Pulse AP did not change appreciably. The EMG showed appearance of bioelectric activity in the tested muscles, which constituted 30-50% of the maximum before exposure to accelerations.

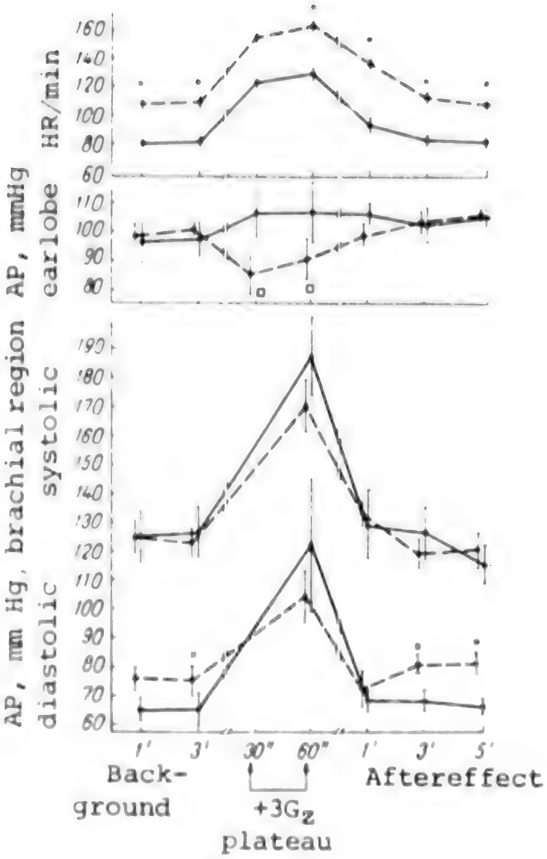

Figure 1.
Dynamics of cardiovascular system parameters during exposure to head-pelvis G forces of +3 G_z for 60 s in healthy subjects, 41-49 years of age, before (solid line) and after (dash line) 7-day immersion. Here and in Figures 2 and 3:
*$P<0.05$
×$P<0.1$
box--$P<0.2$

During the aftereffect period, there was a tendency ($P<0.1$) toward decline of CO, SV and increase of TPR ($P<0.2$). There was increase of f and $\dot{V}$, decrease in V_T, increase in $\dot{V}O_2$ (by 14%) and oxygen debit.

After immersion, all of the subjects endured +3 G_z for 60 s satisfactorily. Their vision was clear.

There was the same direction of changes in parameters of the cardiovascular system as before immersion, but they were considerably more marked (Figure 1). At the +3 G_z plateau, HR increased to an average of 161/min, which was 25% above the rate during practice rotations. Two subjects presented isolated extrasystoles of the ventricular type. AP in the earlobe vessels constituted a mean of 90 mm Hg, which was 15% lower than with rotation before immersion. The pulse amplitude of earlobe vessels diminished to the isoelectric line in 1 subject 3 s before the end of exposure, and recovered only during deceleration of the centrifuge. For 3-5 min of the recovery period after stopping the centrifuge we observed a tendency ($P<0.2$) toward decline of pulse pressure due to elevation of diastolic AP ($P<0.05$). As compared to prerotation data, there was a decrease in SV (by 33%), CO (by 15%) and increase in TPR (by 4%) 40-50 min after stopping the centrifuge (Figure 2).

The changes in parameters of external respiration during exposure to accelerations before and after immersion were in the same direction, but in the latter case the relative change and absolute values were more marked. Thus, the average f on the plateau was 31% greater after immersion than before (Figure 3). In the aftereffect period, there was slower restoration of external respiration parameters after immersion than before. Thus, $\dot{V}$ returned to the base level in the 2d min before immersion and 4th-5th min after immersion. For the first 5 min of the aftereffect period, $\dot{V}O_2$ was 26% higher than the base levels. All this is indicative of the fact that a larger oxygen debit develops during the period of exposure to accelerations after immersion.

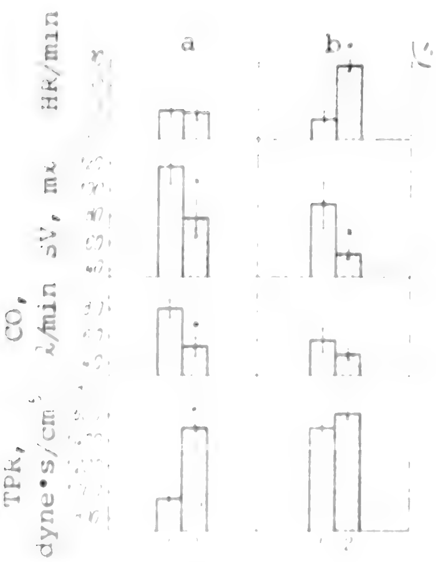

Figure 2.
Dynamics of cardiovascular system parameters of healthy subjects, 41-49 years old, before (40 min prior; a) and after (40 min after; b) exposure to +3 G_z for 60 s, before (1) and after (2) 7-day immersion

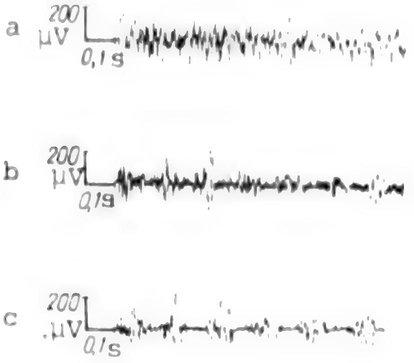

Figure 4.
Right soleus EMG dynamics during exposure to +3 G_z for 60 s in subject K.

a) after 15-s exposure--interference EMG
b) after 35-s exposure--tendency toward grouping of EMG oscillations
c) after 48-s exposure--alternation of groups of EMG oscillations and periods of bioelectric silence ("fatigue tremor")

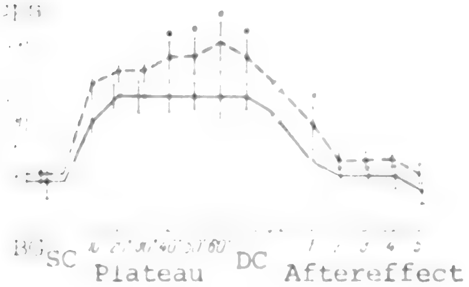

Figure 3.
Dynamics of respiration rate with exposure to +3 G_z in older subjects before (solid line) and after (dash line) 7-day immersion

Key:
BG) background
SC) starting centrifuge
DC) deceleration of centrifuge

Comparative analysis of the EMG before and after immersion revealed a tendency toward increase in bioelectric activity of tested muscles after immersion. Two subjects presented grouping of EMG oscillation and alternation of oscillation groups with periods of bioelectric silence (Figure 4) prior to termination of accelerations. The frequency of oscillation groups constituted 5-7/s. Such EMG changes are known in the literature under the name of "fatigue tremor" [8], and they characterize some decline of functional reserve of skeletal muscles after immersion.

Thus, our data are indicative of diminished endurance of accelerations by older individuals after 7-day immersion. These changes were probably due to development of deconditioning of different functional systems with simulation of weightlessness in the laboratory.

A comparison of our findings to data in the literature [9-11] shows that the direction and severity of physiological changes due to exposure to +3 G_z accelerations before and after immersion in subjects 41-49 years of age showed no appreciable differences from the reactions of younger subjects (23-36 years) to similar factors.

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HUMAN EXTERNAL RESPIRATION AND GAS EXCHANGE IN ACUTE PERIOD OF ADAPTATION TO IMMERSION IN WATER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 13 Mar 81) pp 43-46

[Article by O. L. Golovkina]

[English abstract from source] Responses of respiration and gas exchange of 6 test subjects to 3-day dry immersion were investigated. It was found that an exposure to immersion was accompanied by decreases in respiratory volume, vital lung capacity, maximum pulmonary ventilation, and breathing time retention during inhalation and expiration. These changes were paralleled by an increase in the portion of the functional dead space and a decrease in the portion of the efficient alveolar volume. The permeability of respiratory tracts remained unchanged. These changes seem to be of the type of total respiratory insufficiency induced by circulatory disorders. This may be one of the factors responsible for a decline in human tolerance to exercises and acceleration applied after an exposure to simulated weightlessness.

[Text] The acute period of man's adaptation to weightlessness is associated with functional changes in several of the body's systems, in particular, external respiration and exchange of gases [1, 2]. Submersion in a water-immersion medium is one of the methods that simulates best conditions of real weightlessness. Immersion is associated with redistribution of blood to the upper part of the body and plethora in the pulmonary circulatory system [2-4]. This causes reduction of alveolar lumen, worsening of conditions for exchange of gases and alveolar ventilation. The observed changes may be among factors that worsen endurance of subsequent factors, in particular, accelerations [5, 6].

Our main objective here was to assess changes in man's external respiration and gas exchange in a water immersion environment.

Methods

A total of six subjects 28-32 years of age participated in these studies. They were examined before and during immersion lasting 3 days, which was of the "dry" submersion type [7].

Examination included registration of heart rate (HR), pneumotachogram, spirogram, and several functional tests on the system of external respiration; we examined exhaled alveolar and mixed air. The results were submitted to statistical processing, and differences were considered reliable at $P \leq 0.05$. The Table lists the results of these studies. Volumetric parameters are expressed in the BTPS system and those for gas exchange in the STPD system.

Dynamics of parameters of external respiration and gas exchange in studies involving 3-day water immersion (M±m)

Tested parameter	Background	Day of immersion		
		1	2	3
HR/min	61±3,30	54±3,10	57±3,20	62±3,40
f, cycles/min	10±1,40	13±1,50	14±1,60	12±1,50
V, ℓ/min	9,33±0,04	10,05±0,01	10,34±0,04	9,82±0,04
IRV, ℓ	3,29±0,02	3,23±0,02	2,89±0,02	2,70±0,02
ERV, mℓ	778,5±9,68	742,6±11,92	875,4±12,75	890,4±12,86
IC, ℓ	4,36±0,03	4,04±0,03	3,69±0,03	3,59±0.03
VC, ℓ	5,32±0,03	4,84±0,03	4,48±0,03	4,59±0,03
FEV_1, ℓ	4,20±0,03	3,90±0,03	3,81±0,03	3,59±0,03
V_{max}, ℓ/min	122,03+4,75	119,06±4,68	111,89±4,56	107,49±4,47
FR, ℓ	112,7±4,56	109,0±4,48	101,55±4,35	97,67±4,26
VO_2, mℓ/min	317,20±7,65	298,93±7,41	301,76±7,51	293,72±7,35
VCO_2, mℓ/min	272,27±7,08	264,90±7,06	262,21±7,00	247,03±6,76
EE, kcal/min	1,54±0,04	1,47±0,04	1, 7±0,01	1,43±0,04
P_ACO_2, mm Hg	38,94±2,67	37,91±2,63	35,71±2,56	35,55±2,55
V_T, mℓ	1068,56±14,19	810,65±12,30	804,31±12,33	895,98±12,98
VD_f, mℓ	257,0±6,98	225,98±6,55	207,57±6,24	237,34±5,99
VA_{eff}, mℓ	711,56±11,71	484,67±9,51	496,73±9,87	558,6 ±10,36
VD_f/V_T, %	24,05	27,88	25,81	26,49
VA_{eff}/V_T, %	66,59	59,79	61,76	62,35
[illegible]	95±4,19	84±3,97	82±3,89	87±4,03
[illegible]	30±2,45	27±2,31	24±2,20	22±2,03

Results and Discussion

The parameters of external respiration and gas exchange obtained in the background period, with the subjects in horizontal position conformed to normal values.

During immersion at rest, in horizontal position, the subjects reported some breathing difficulty, heaviness and tenderness of chest muscles upon deep inspiration.

During immersion, minute volume ($\dot{V}$) increased by 7.7% on the 1st day, 10.8% on the 2d and 5.2% on the 3d day, as compared to background levels.

Tidal volume (V_T) constituted 75.9% of background value on 1st day, 75.3% on the 2d day and 83.8% on the 3d.

Frequency of respiratory excursions (f) increased.

Inspiration reserve volume (IRV) did not change on the 1st day, constituting 87.7 and 81.9% of background values on the 2d and 3d days, respectively.

Expiration reserve volume (ERV) constituted 95.4% of background value on the 1st day, 112.5% on the 2d and 114.4% on the 3d.

Inspiration capacity (IC) was 92.5% on the 1st day, 84.6% on the 2d and 82.4% on the 3d.

Vital lung capacity (VC) and forced vital capacity per second (FEV_1) diminished during the test period. On the 1st day, VC constituted 91.0% of background value, on the 2d it was 84.3% and on the 3d 86.3%. FEV_1 constituted 93.0, 90.7 and 85.5%, respectively. Statistically reliable differences were also demonstrated between parameters on different days of the study.

Maximum lung volume ($\dot{V}_{max}$) and respiratory reserve (RR) had a tendency toward decline during the study.

With relative stability of HR, oxygen uptake $\dot{V}O_2$, carbon dioxide output ($\dot{V}_{CO_2}$) and energy expenditure (EE) changed mainly with regard to spirometric parameters. IC, $\dot{V}$ and V_T reached the most change on the 1st-2d days of immersion, with a tendency toward normalization on the 3d day. IRV, ERV, VC, FEV_1, $\dot{V}_{max}$ and RR showed the most changes by the 2d-3d days of immersion. Evidently, the observed dynamics of the parameters is a consequence of redistribution of blood into the chest, plethora in the system of pulmonary circulation and decrease in intrapulmonary volumes [8, 9]. The fact that no changes were demonstrable in the course of the functional breathing tests characterizing degree of patency of the respiratory tract is indicative of restrictive processes in the lungs [10].

The observed changes in lung volumes were associated with a reduction in time of voluntary apnea by the 2d day of immersion by 13.7% in inspiration (ta_i) and 20.0% in expiration (ta_e), as compared to background levels, with further decline on the 3d day.

Partial carbon dioxide pressure in alveolar air (P_ACO_2) had a tendency toward decline during the entire immersion period. In the presence of decrease in V_T during the study and increase in f, the absolute volume of functional dead space (VD_f), which was calculated using the equation of Bohr, and effective alveolar volume VA_{eff} diminished. VD_f constituted 87.93, 80.77 and 92.35% on the 1st to 3d days, while VA_{eff} constituted 68.11, 69.81 and 78.51%, respectively. However, there was more marked decline of VA_{eff} than VD_f. When comparing VD_f and VA_{eff} to V_T, the share of VD_f in V_T increased during immersion while that of VA_{eff} decreased. Such dynamics of the parameters is indicative of diminished efficiency of alveolar ventilation and worsening of ventilation-perfusion inequality [8, 9, 11, 12].

The fact that some of the parameters of the system of external respiration had some tendency toward background values on the 3d day of immersion could apparently be attributed to adaptation, as well as emotional reaction to impending termination of the experiment.

Thus, the changes in parameters of external respiration and gas exchange in subjects during 3-day water immersion indicate that disturbances develop from the first day, which could be the result of redistribution of blood to the upper parts of the trunk and plethora of the system of pulmonary circulation, which could be associated with an increase in load on the right heart. Probably, expressly the static signs in the lungs lead to decline of functional capacity of the external respiration system--increase in rigidity of pulmonary tissue, increased resistance to respiration in inspiration, enlargement of functional dead space, decrease in effective alveolar ventilation, impairment of ventilation-perfusion relations and diminished oxygenation of blood. The observed functional changes in external respiration and gas exchange are not associated with impairment of patency of the airways, and they occur on the order of total respiratory insufficiency apparently caused by circulatory disturbances [10, 13].

The above changes in human external respiration and gas exchange during immersion may be among the causes of diminished resistance to subsequent functional loads and G overloads.

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REACTION TO DIMINISHED CIRCULATING BLOOD VOLUME IN INDIVIDUALS WHO ARE SUSCEPTIBLE AND INSUSCEPTIBLE TO MOTION SICKNESS (SEASICKNESS)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 3 Feb 81) pp 46-49

[Article by V. G. Isupov, D. G. Maksimov and B. I. Polyakov]

[English abstract from source] The study of 54 healthy male test subjects demonstrated significantly different responses of motion sickness susceptible and resistant people to 10-minute occlusion of their femoral veins. The changes in limb rheograms, as well as heart rate and stroke volume indicated that in motion sickness susceptible subjects the circulating blood volume in the upper body decreased, whereas in motion sickness resistant subjects it remained unaltered or increased in response to the occlusion.

[Text] It was previously shown [1, 2] that hemodynamic disturbances with redistribution and reduction of circulating blood volume are among the pathogenetic factors of motion sickness (MS). At the same time, reduction of circulating blood volume is associated with vestibular reactions [3].

It can be assumed that resistance to MS is related to the nature of compensatory and adaptive reactions of the cardiovascular system. If this is so, the differences between susceptible and insusceptible individuals with regard to the above reactions should be manifested not only with motion, but decrease in circulating blood volume due to other causes.

Our objective here was to compare the hemodynamic reactions to a decrease in circulating blood volume induced by occlusion of femoral veins in subjects with high and low resistance to MS.

Methods

We tested 29 people with high (first group) and 25 with low (second group) levels of vestibulovegetative stability (VVS).

VVS was determined by the method of I.I. Bryanov [4]. The veins of the lower extremities were occluded for 10 min by means of pneumatic cuffs applied over the proximal segments of the thighs. Cuff pressure was 5-10 mm Hg higher than systolic pressure.

Before and during occlusion, we recorded rheograms using three regional leads: right frontomastoid, forearm and lower leg. Stroke volume of the heart (SV) and minute volume of circulation (MV) were determined using a right wrist--left ankle integral lead and calculations were made with the formula of A. A. Kedrov [5].

The rheograms were taken before occlusion and periodically during occlusion.

We examined the following parameters to assess vascular tonus and hemodynamics in the regions studied: pulsed filling, on the basis of the rheographic index (RI) [6]; tonus of large arteries, according to ratio of second to first systolic wave (modification of elasticity parameter) [7]; tonus of arterioles and precapillaries, according to ratio of amplitude at the level of the incisura to maximum systolic wave (dicrotic index) [8]; venous resistance, according to ratio of amplitude of dicrotic wave to maximum systolic wave (diastolic index--DI) [9].

Results and Discussion

During occlusion of veins of the lower extremities, the changes in most parameters studied reached maximum levels in the 5th-7th min. Thereafter, there was stabilization or partial restoration of parameters.

Tables 1 and 2 show that individuals with high VVS presented reliably higher mean values for heart rate (HR), MV, parameters of tonus of small arterial vessels and resistance of veins of the head.

Table 1. Changes in HR, SV adn MV under the influence of occlusion of veins of lower extremities in first and second groups of subjects

Hemodynamic parameter	Base values		Occlusion (5th-10th min)	
	group			
	1	2	1	2
HR	62±1.2	57±1,5*	65±1,2	55±1,5*
SV	72±2,5	72±2,7	63±1,7	63±3.1
MV	4.56±0,13	4,18±0,10*	4,03±0.11	3.51±0,15*

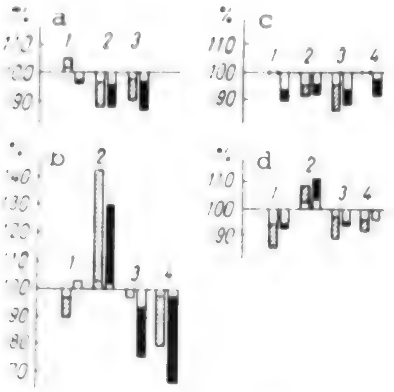
Note: Here and in Table 2, asterisk refers to $P<0.05$.

During occlusion of veins of the lower limbs, there was the same decrease in SV in both groups of subjects. HR increased somewhat in the first group and decreased in the second. As a result, there was more marked decline of MV in the second group of subjects (see Figure, a).

There was an increase in tonus of large vessels of the leg in both groups. A more marked reaction was observed in the first group of subjects (see Figure, b). In the same group, we observed a decrease in pulsed filling of the crus, which was reliably lower in the 7th-10th min of occlusion than in the second group (see Table 2). There was reliable decrease in tonus of small crural arteries only in the second group. The same group of subjects presented more marked decrease in resistance of veins.

Table 2. Changes in rheographic parameters of first and second groups of subjects under the influence of occlusion of lower limb veins

Rheographic parameter	Region examined	Base values		Occlusion(5-10th min)	
		group			
		1	2	1	2
Rheographic index	Leg	0,63±0,02	0,66±0,03	0,57±0,03	0,68±0,04*
	Arm	0,44±0,03	0,44±0,03	0,44±0,02	0,40±0,03
	Head	1,14±0,07	1,29±0,08	0,99±0,06	1,21±0,08*
Tonus of large arteries	Leg	0,57±0,02	0,61±0,01	0,81±0,02	0,79±0,02
	Arm	0,66±0,03	0,63±0,03	0,61±0,04	0,58±0,01
	Head	0,87±0,02	0,82±0,03	0,95±0,03	0,92±0,03
Dicrotic index	Leg	0,29±0,01	0,30±0,02	0,30±0,02	0,22±0,03*
	Arm	0,43±0,02	0,43±0,03	0,37±0,03	0,38±0,02
	Head	0,67±0,02	0,59±0,03*	0,60±0,03	0,56±0,02
Diastolic index	Leg	0,38±0,01	0,38±0,01	0,30±0,02	0,25±0,03
	Arm	0,61±0,03	0,71±0,04	0,61±0,02	0,66±0,03
	Head	0,76±0,03	0,67±0,03	0,70±0,03	0,64±0,03



Reactions (% of base value) of some parameters of the cardiovascular system of subjects in the 1st (striped columns) and 2d (black) groups in 5th-10th min of occlusion of femoral veins. Y-axis, indicators of change (%). Unmarked columns refer to mean-square error of base data

a) changes in HR (1), SV (2), MV (3)
b,c,d) changes in pulsed filling (1), tonus of great arteries (2), tonus of small arteries and arterioles (3) and venous resistance (4) in crural, brachial and head regions, respectively

In the forearm region, pulsed filling and venous resistance during occlusion were close to base levels in the first group, whereas in the second group they dropped by 8-10%. At the same time, there was about the same degree of decrease in tonus of great arteries and precapillaries in both groups of subjects (see Figure, c).

In the head region (see Figure, d), the reaction consisted of decrease in pulsed filling, tonus of small arteries and venous resistance. These changes were more marked in the first group of subjects, which led to a decrease in intergroup differences in tonus of precapillaries and venous resistance (see Table 2). There was about the same increase in tonus of great arteries.

These data are indicative of qualitative differences between the first and second groups of subjects with respect to hemodynamic reactions to the test with diminished MV. The differences consisted of the fact that pulsed filling diminished in the bottom part of the body (crural RI) and did not change in the top part (forearm RI) in the first group of subjects during the test. At the same time, the second group presented opposite signs: decrease in pulsed filling of brachial vessels and no change in the leg. This apparently occurred as a result of more significant increase in tonus of great arteries of the lower extremities of subjects in the first group, with unchanged tonus of precapillaries. However, in the second group, the less marked increase in tonus of large arteries was associated with decrease in precapillary tonus, as well as more significant decrease in venous tonus than in the first group.

The demonstrated distinctions of cardiovascular system reactions in the first and second groups of subjects can apparently be attributed to higher tonic activity of the sympathoadrenal system in the first group [10]. Hence the greater MV in this group of subjects. The tendency toward increase in HR, more marked increase in tonus of major arteries of the leg, as well as greater initial tonus of small arterial vessels of the head and higher initial HR in subjects of the first group [11], are in favor of this assumption.

The concurrent decrease in precapillary tonus and venous resistance in the upper and lower extremities of subjects in the second group could also be explained from this point of view. Probably, these changes are related to opening of arteriovenous anastomoses, which are called upon to increase return of blood to the heart [12]. If we consider that arteriovenous anastomoses are the most catecholamine-sensitive element of the microcirculatory system [13], it can be assumed that the second group of subjects had more open anastomoses.

Thus, the reaction of the cardiovascular system of the first group of subjects can be considered better. Since the decrease of SV was associated with increase of HR, while pulsed filling of the upper part of the body remained unchanged in the first group, we could expect stabilization of circulating blood volume in their upper body on the base level or even an increase in the first group. In the second group, the decrease in SV was associated with decrease in pulsed filling of the upper body and decrease of HR, which probably led to reduction of circulating blood volume in the upper parts of the body.

The (Shval'm) occlusion test is used in functional diagnostics to assess hemodynamic regulation. At the same time, as shown by our studies, this test also permits evaluation of compensatory and adaptive reactions of the cardiovascular system to a decrease in circulating blood volume in individuals differing in vestibulovegetative stability.

The results of this study confirm the desirability of using the occlusion test in aerospace medical practice [14]. A period of 5-7 days should be considered best for duration of occlusion.

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EFFICACY OF KAVINTON IN PREVENTION OF MOTION SICKNESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 23 Apr 81) pp 49-51

[Article by D. Bodo, A. R. Kotovskaya, R. R. Galle, L. N. Gavrilova, G. A. Gusakova and V. A. Smirnov (Hungarian People's Republic and USSR)]

> [English abstract from source] The effectiveness of the Hungarian drug kavinton used to prevent motion sickness was assessed. During the study 8 motion sickness susceptible test subjects were kept in a chamber rotating at a rate of 6 rpm for 5 hours. The effectiveness of the drug taken regularly during the exposure was compared with that of scopolamine and placebo taken as a single dose. The results obtained are suggestive of a positive effect of kavinton as an antimotion drug.

[Text] The first stage of man's adaptation to weightlessness is not infrequently associated with development of functional disturbances, which were called the space form of motion sickness (SFMS). For this reason, many authors conducted work to find pharmacological agents for the prevention and treatment of SFMS. Unfortunately, no reliable means of preventing and treating SFMS have yet been found. This is largely attributable to the absence of clearcut ideas about the causes and mechanisms of development of this disease, as well as use in ground-based studies of models that do not adequately represent SFMS.

The state that develops when man spends a long active time in slowly revolving systems is considered the most adequate ground-based model of SFMS [2].

Hemodynamic changes, in particular circulatory disturbances of cerebral vessels, may be of some significance to the genesis of motion sickness (MS). On this basis, studies were conducted, with positive results, of the effects on development of MS under model conditions of a Hungarian drug, kavinton, during use of brief vestibular factors. Kavinton is an agent that selectively improves cerebral circulation, cerebral trophics and augments the energy potential. It is well tolerated by patients and has virtually no side-effects.

This study is concerned with the efficacy of a course of kavinton as a means of pharmacological prevention of MS, which occurs when man is submitted to long-term slow rotation.

Methods

Our studies involved rotation of subjects in a special chamber placed on the arm of a centrifuge close to the axis of rotation. The chamber (1.2×1.8×2.0 m in size) was equipped with lighting, ventilation, communication systems and a television camera to monitor the condition of the subjects, as well as a system of taking and transmitting physiological information. There were two chairs in this chamber. We used rotation at the rate of 6 r/min for 5 h. The subjects performed specific tasks during rotation, which involved moving about the chamber. The subjects performed a series of graded head movements every hour as a standard vestibular load.

Each pair of subjects participated in 4 rotation sessions at 2-week intervals. As shown by preliminary tests, such an interval was sufficient to preclude the effect of prior rotation on intensity of MS. The first rotation (background) was used for initial evaluation of severity of MS. The subjects were given a placebo 3 times a day for 7 days prior to the second rotation, with replacement of the last dose with scopolamine in a dosage of 0.6 mg 30-40 min before the start of rotation. Before the third rotation, the subjects took only a course of placebo, and before the fourth they took kavinton, at the rate of 10 mg, 3 times a day, for 1 week.

Eight men, 26-39 years of age, with low initial vestibular stability, participated in these tests.

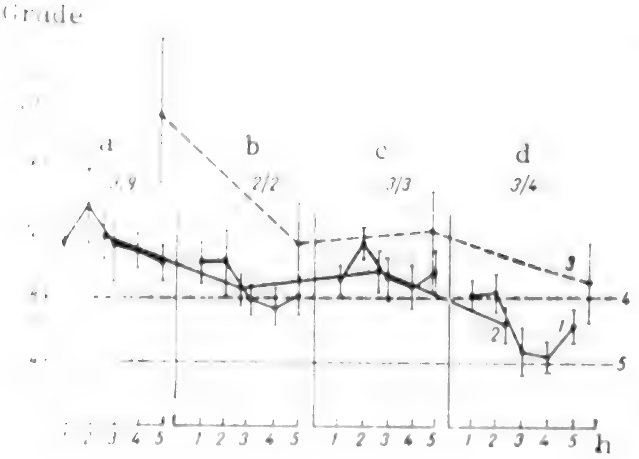
We used the method of grading to determine severity of MS. Each symptom of MS (vertigo, pallor, perspiration, nausea, etc.) was given a grade of 1-2 or 4, depending on severity. The total of all grades for all symptoms (maximum for each symptom) occurring in 1 h characterized the severity of MS for that hour of rotation. The mean hourly grade was used as an indicator of severity of MS as a whole for the entire 5-h period of rotation. In addition, we recorded frequency of vomiting, overall (5-h) grade for nausea, as well as subjective assessment of endurance of rotation by the subjects.

Results and Discussion

In the background test, all of the subjects presented distinct manifestations of MS throughout the period of rotation. Three people had 9 vomiting episodes during the rotation period. Accordingly, they had a high overall grade for nausea, which fluctuated from 7 to 40 and constituted a mean of 19.1±4.4 (see Figure, a).

There was individual variation from moderate to severe MS syndrome; however, the average overall grade for each hour of rotation reliably exceeded 8, which is an indication of severe MS. The average 5-h grade constituted 6.2 in only one subject; for all the rest it exceeded 8 and constituted 11.5±1.2 for the entire group. On the whole, endurance of rotation was assessed as poor in seven men, on the basis of severity of MS, and satisfactory in one.

Intake of scopolamine diminished manifestations of MS quite distinctly. The number of vomiting episodes decreased to two in two men. Overall grade for nausea decreased for six people, did not change in one and increased somewhat in another subject. The average overall grade dropped by 40% under the influence of scopolamine (see Figure, b).



Severity of MS (grade) during 5 h of rotation at the rate of 6 r/min. X-axis, duration of rotation (hours); y-axis, grade given to MS

a) background c) placebo
b) scopolamine d) kavinton
1) overall grade for each hour of rotation (M±m)
2) average grade for 5 h (M±m)
3) overall grade for nausea symptom over 5 h (M±m)
4) range of severe MS
5) range of moderate MS
3/9--number of subjects/number of bouts of vomiting

The grade for severity of MS syndrome dropped reliably, as compared to background data, starting in the 3d h of rotation; however, it was not reliably below a grade of 8 (range for severe MS). The average grade dropped to 4 in 2 cases and remained above 8 in the others. On the average, this parameter decreased by about 27%, as compared to the background level.

On the whole, in spite of the positive effect of scopolamine, it should be stressed that this effect was of practical significance in only two subjects: endurance of rotation improved distinctly after intake of scopolamine (the grade for severity of MS did not exceed 5). However, on the average for the group, the manifestations of MS persisted at the level of severe ones, in spite of reliable decrease of nausea syndrome. Apparently, this can be attributed to the side-effects of scopolamine.

The nausea syndrome was less marked in seven men, as compared to the background study, after a course of kavinton, but less marked than after intake of scopolamine in four cases. The average overall grade for nausea dropped reliably, by almost 60% when compared to background data and 23% when compared to the effect of scopolamine (see Figure, d).

The severity of the MS syndrome was reliably lower than in the background tests over the entire period of rotation and, starting with the 3d h it was reliably lower than 8. The average grade dropped in comparison to base value in all subjects, and was less than 8 in 6 of them. In five subjects, this parameter was lower than in the tests with scopolamine. The average grade given to this parameter for the group was reliably lower than 8, i.e., it dropped by 45%, as compared to base data, and by 26%, as compared to intake of scopolamine.

Our analysis offers rather convincing evidence of the beneficial effect of kavinton in preventing MS, which occurs when man spends a long and active time in a rotating system.

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NYSTAGMOMETRY OF OPTOVESTIBULAR INTERACTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 28 Jul 81) pp 51-55

[Article by M. M. Levashov and A. I. Tumakov]

[English abstract from source] Nystagmograms recorded in healthy people (270 ENG from 30 children, aged 3 to 7) were analyzed quantitatively. The velocity of the slow component of the vestibular nystagmus during caloric tests, optokinetic nystagmus in response to stimul applied at 20 and 10°/sec, as well as vestibulooptokinetic nystagmus resulting from modulation of the optokinetic nystagmus due to the inhibitory or enhancing effect of caloric stimulation were measured. The modulation level, i.e., the change of the velocity of the slow component that accompanied the transition of the optokinetic nystagmus to the vestibulo-optokinetic nystagmus, was always less than that of the vestibular nystagmus. This disagrees with the concept about algebraic summation of intensities of the reactions. The modulation level showed a low correlation with the vestibular nystagmus slow component velocity and depended on the optokinetic nystagmus velocity: at 10°/sec the inhibitory effect was smaller than the enhancing one, and at 20°/sec the situation was the opposite. At 20°/sec the slow component velocity was twice higher than at 10°/sec. It is therefore suggested that the parameter reflects the level of the residual activity of the optokinetic system which is independent of vestibular afferentation.

[Text] Vestibulo-optokinetic nystagmus (VOKN), generated by a hypothetical system in which the mechanisms of vestibular (VN) and optokinetic (OKN) nystagmus are contained as components (i.e., subsystems), is usually formed when there is coordinated interaction of the latter [1]. In conflict situations, when visual and vestibular signals are contradictory, VOKN also occurs, and investigation of its distinctions could yield some interesting information about the mechanisms of interaction between the optic and vestibular systems. Knowledge of these mechanisms is needed not only by physiologists, but specialists in applied otoneurology [2].

In this study, we artificially aggravated the conflict between subsystems in order to demonstrate factors that are important to gain an idea about the functional patterns of the vestibulo-optokinetic system (VOKS). Our objective was to examine distinctions of VOKN formed under conditions where vision gives signals about displacement of the visual environment in the plane of the lateral semicircular canals, the receptors of one of these canals report "rotation" of the head and the receptors of the other one send afferentation corresponding to the resting level. Such conditions were created by means of monaural cold stimulation against the background of OKN in two directions.

We must make some comments about OKN. In view of the high degree of corticalization of visual function, the role of the cortex in forming OKN becomes so significant that some researchers deny the existence of subcortical OKN in man, in the belief that it was completely lost in the course of phylogenesis [3]. However, there is also a different point of view [4]. Involvement of the cortex in forming OKN can be reduced to a minimum if the attention of an adult subject is distracted from tracking an optokinetic stimulus in order to actively solve a different problem, for example, mental arithmetic. The distinctions of OKN that appear under such conditions enable us to assess it as being subcortical. In order to obtain stable optokinetic reactions in testing children [5], it was sufficient to replace the traditional "striped" optokinetic pattern with a "polka dot" one (round white spots 7° in diameter scattered at random over a black background) and enlarge the size of the screen (120×70°). Under such conditions, it was not necessary to give any instructions whatsoever, and a distinct, regular OKN appeared in all of the children. For this reason, it can be assumed that, with respect to its mechanisms, this nystagmus was closer to subcortical reactions than cortical ones.

Methods

To examine the mechanisms of interaction between VN and OKN it was desirable to have the latter as close as possible to the subcortical form. We examined 30 children (3 to 7 years of age) who presented no otiatric problems.

The caloric test (30°C, 100 mℓ) was performed on the right ear. The subject was on a stand that provided for backward inclination in the sagittal plane to an angle of 60°, and he could see the optokinetic screen in a mirror. We recorded 9 electronystagmograms (ENG) on each subject: horizontal VN to the left with cold test to the right (1 ENG); OKN to the right and OKN to the left with two optokinetic stimuli (OKS)--20 and 10°/s (4 ENG); VOKN with cold tests to the right performed against the background of each OKN (4 ENG). To determine the intensity of nystagmus, we calculated the product of mean frequency multiplied by mean amplitude, obtaining a characteristic with the dimensionality of slow component velocity and a value close to it (in describing our results, this characteristic is referred to as SCV). For assessment of caloric nystagmus, we used a segment of culmination of nystagmus, choosing an ENG segment of about 20 s; to assess OKN, we selected a segment of the same duration. We designated the initial (background) OKN as nystagmus to be modulated, caloric VN as modulating and the results of interaction (i.e., VOKN) as modulated nystagmus. When the directions of nystagmus subject to modulation and modulating nystagmus coincided, the resultant reaction was referred to as VOKNC, if they did not coincide--VOKNN, i.e., as adopted in [1].

Results and Discussion

The monaural cold test elicited a change in SCV of OKN subject to modulation. Table 1 lists the results of modulation with a 20°/s stimulus. The arithmetic mean for the sample of SCV VOKNCl was reliably greater than the means in samples SCV OKNl and SCV OKNr (subscripts "l" and "r" refer to direction of nystagmus). There was no reliable difference in arithmetic means between SCV VOKNNr and SCV OKNr, but the decrease in intensity is reliable according to the sign criterion. As a result of modulation there appears reliable asymmetry of nystagmus directed to the right and left (the determination is made according to the diagnostic rule in [3]). The arithmetic mean absolute difference between SCV VOKNCl and SCV VOKNNr constituted 12°/s, while the mean of relative asymmetries, i.e., 100·(SCV VOKNCl - SCV VOKNNr)/(SCV VOKNCl + SCV VOKNNr), reached 30%.

Table 1.
Statistical processing of nystagmometric data--SCV(°)/s of nystagmic reactions
OKS 20°/s

Nystagmus	$\bar{x}$	σ	m	CV, %
KNl	12,67	1,90	0,68	15,03
OKNl	19,82	1,02	0,37	5,15
OKNr	19,68	1,43	0,51	7,29
VOKNCl	26,46	2,56	0,77	8,15
VOKNNr	14,48	1,13	0,55	10,53
$a - b$	0,15	1,26	0,45	—
$\frac{a - b}{a + b}$	0,001	0,032	0,012	—
$b - d$	5,20	2,15	0,77	41,32
$c - a$	6,63	2,33	0,84	35,16
$c - d$	12,00	3,15	1,12	—
$\frac{c - d}{c + d}$	0,292	0,071	0,025	—

Table 2.
OKS 10°/s

Nystagmus	$\bar{X}$	σ	m	CV, %
KNl	12,67	1,90	0,68	15,03
OKNl	10,36	1,19	0,43	11,45
OKNr	10,38	1,43	0,51	13,91
VOKNCl	1 ,51	2,09	0,75	13,49
VOKNNr	6,97	1,07	0,38	15,42
$a - b$	0,08	1,57	0,56	—
$\frac{a - b}{a + b}$	0,006	0,078	0,028	—
$b - d$	3,32	1,54	0,55	46,35
$c - a$	[illegible],15	2,63	0,94	51,07
$c - d$	8,54	2,51	0,90	—
$\frac{c - d}{c + d}$	0,378	0,091	0,033	—

In both tables: KNl) caloric nystagmus to the left
a, b) OKNl and OKNr, respectively
c, d) VOKNCl and VOKNNr

The results were qualitatively the same with OKS of 10°/s (Table 2). The reliability of the modulating effect was confirmed by the sign criterion. The absolute difference in SCV constituted a mean of 8.5°/s and relative difference was 37.8%.

The opinion of some authors has been disseminated (see, for example, [6]). to the effect that interaction occurs by the principle of simple algebraic addition of intensity of two nystagmuses, but we were unable to confirm this view under the above-described conditions. At various mean intensities of modulation of OKN, the same vestibular stimulus has a different modulating effect: with lower OKS there was less marked inhibitory modulation. In spite of the fact that with OKS of 10°/s, the mean intensity of modulated OKN (SCV =

12°/s), the mean intensity of inhibited nystagmus, i.e., SCV VOKNN, was unexpectedly high (about 7°/s). Another interesting fact was discovered: with OKS of 20°/s, overall depth of modulation (i.e., mean difference between SCV VOKNCl and SCV VOKNNr) was found to be approximately equal to the mean intensity of modulating VN. The results of studying the correlations are listed in Tables 3 and 4.

Table 3.
Correlation between intensity (SCV) of different forms of nystagmus at OKS of 20°/s (a) and 10°/s (b)

Compared nystagmus	Coefficient of correlation	
	a	b
OKNr and OKNl	0,514	0,296
VOKNCl and VOKNNr	—0,437	—0,173
OKNr and KNl	—0,129	0,297
OKNl and KNl	—0,342	0,106
VOKSl and KNl	—0,159	0,406
VOKNNr and KNl	0,166	0,148
KNr and VOKNCl-VOKNNr	0,190	—0,275
OKNr-VOKNNr and KNl	—0,204	0,173
VOKNCl-OKNl and KNl	0,005	0,275
OKNr-VOKNNr and OKNr	0,703	—0,117
VOKNCl-OKNl and OKNl	—0,386	—0,189

With OKS of 20°/s, the most important data (see Table 3) amount to the following. The initial OKN are correlated, but the correlation is not marked. Intensity of modulating VN is not the deciding factor for depth of the modulating (inhibitory or enhancing) effect. The depth of modulation is related to intensity of modulated OKN. The more intense the modulated OKN, the stronger the inhibitory effect. There is a negative correlation between the enhancing effect and intensity of modulated nystagmus. A negative correlation is observed between modulated reactions, i.e., between SCV VOKNC and SCV VOKNN. Only the modulated OKN in the same direction (OKNl) had a mild relation to modulating nystagmus (VNl), while other reactions (i.e., OKNr, VOKNNr and VOKNCl) were not correlated with VNl. Such results were obtained with rather intensive OKS.

At lower OKS (10°/s), the results were qualitatively similar (see Table 4), but we demonstrated two exceptions. The first is referable to the link between modulating VN and VOKNC. Such a link was demonstrated with lower OKS: the greater the SCV of VN, the greater the SCV of VOKNC. The second exception is referable to correlation between modulated nystagmus (OKN) and depth of inhibitory effect. Unlike what we observed with OKS of 20°/s, the depth of inhibitory effect at OKS of 10°/s was found to be unrelated to the intensity of the initial OKN.

We also made a search for the statistical relations between the same reactions with two different OKS. Unlike the preceding problem, where we studied the relationship between samples obtained at the same intensity of OKS, in this case we tried to answer a different question: to what extent are the quantitative changes in nystagmus, caused by the modulating effect of an additional vestibular stimulus, associated when OKS are different? The answer turned out to be unexpected: such relations are problematic and, perhaps, nonexistent. We were unable to obtain convincing evidence of correlations, even in cases where links would appear quite natural. In particular, we found no correlation between initial OKN elicited by different stimuli. We found no link between homonymous modulated nystagmus. Nor were there correlations between depths of modulation or extent of relative asymmetry. In other words, the impression was gained that there is a more substantial difference between OKN induced by two different stimuli than a simple quantitative difference in intensity.

Table 4. Correlation between results obtained with two different OKS, 20°/s (a) and 10°/s (b)

Compared nystagmus		Coefficient of correlation
a	b	
OKNr	OKNr	-0.159
OKNl	OKNl	-0.064
VOKNNr	VOKNNr	0.082
VOKNCl	VOKNCl	-0.245
OKNr - VOKNNr	OKNr - VOKNNr	-0.079
VOKNCl - OKNl	VOKNCl - OKNl	-0.197
$\frac{\text{VOKNCl - VOKNNr}}{\text{VOKNCl + VOKNNr}}$	$\frac{\text{VOKNCl - VOKNNr}}{\text{VOKNCl + VOKNNr}}$	-0.229

Note: Nystagmus was assessed according to SCV.

Evidently, this difference was the cause of the above-mentioned exception. We should call attention once more to these discrepancies of results obtained with different OKS: enhancement of nystagmus with OKS 20°/s is unrelated to intensity of modulating VN, but at OKS of 10°/s it is related; the inhibitory effect of the first stimulus is overtly related to intensity of modulated OKN but independent of it with the second.

In spite of the considerable intensity of cold-induced nystagmus, the modulation effect elicited by potential vestibular nystagmus interacting with the background OKN (i.e., enhancement or inhibition of nystagmus) was appreciably less marked than could be expected if the interaction were effected by means of simple algebraic summation of intensities of interacting reactions. Enhancing modulation is manifested to the greater extent if the modulated reaction is less intensive, while inhibitory modulation, on the contrary, is more marked when the modulated nystagmus is more intensive.

These facts indicate that the base state, as well as VOKS activity, are implicated in the modulating effect. There was a possible inhibitory effect only to a certain limit, which could be called the level of residual activity of this system. This level, which can be assessed from the SCV of VOKNN, undergoes a 2-fold change when there is a 2-fold difference in OKS intensity. Since, in this study, the background VOKS activity was directly related to activity of the optokinetic subsystem, it can be considered that, in the presence of the tested conflict, the optokinetic subsystem is more important than vestibular and that a certain part of VOKS activity is independent of the vestibular subsystem.

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EFFECT OF CALORIC STIMULATION OF VESTIBULAR SYSTEM ON HEARING

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 17 Aug 81) pp 55-58

[Article by G. P. Tsurikova]

[English abstract from source] Changes of bone-conduction thresholds for tonal signals (250 and 2000 Hz) in each ear due to caloric vestibular tests were studied in 60 healthy test subjects (32 men and 28 women). These changes were found in 48 subjects. In most cases perceptual thresholds decreased (by 7.3 dB on the average) and in few cases increased (by 8.3 dB on the average). The sign of alteration was independent of the tonal signal frequency or the side exposed to the vestibular test or the number of examinations. The threshold returned to the norm for a long time (30 min or more). These findings suggest that the interaction may be governed by the principles that function in other sensory systems. It is recommended to carry out audiological examinations prior to vestibular tests in order to avoid distortions of the results.

[Text] The vestibular system influences many functions in man. Hearing may also be altered upon stimulation of the vestibular system, as indicated, for example, by measurement of thresholds of air conduction during exposure to angular acceleration. In some cases, the effect of vestibular stimulation enhances auditory sensibility and in others diminishes it [1-3]. The results of the studies of V. G. Bazarov revealed that the direction of the effect may depend on intensity of the vestibular stimulus: mild vestibular stimuli elicited primarily a decline of auditory thresholds while strong ones, on the contrary, depressed auditory sensibility, and the most marked changes occurred with stimulation of otolith organs [4]. Since changes in auditory sensibility may also occur under the influence of stimulation of the visual, olfactory analyzers, proprioceptors and interoceptors, as well as thermocutaneous stimulation [5-10], the demonstrated changes are apparently attributable primarily to central mechanisms.

In addition to central mechanisms, there are probably interreceptor mechanisms of interaction between the vestibular and auditory systems. Such interaction appears to be quite natural, it only by virtue of the close anatomical link that exists between the vestibular system and the cochlea.

Finally, stimuli intended for one receptor may affect an adjacent organ. For example, an acoustic stimulus may have a direct effect on the reaction of the semicircular canals [11]. It has been noted in the literature that auditory sensibility increased (increased duration of perception of tuning fork sounds) after a cold test [12, 13].

Our objective here was to examine the effect of caloric stimulation of the vestibular system on hearing thresholds (according to bone conduction) in essentially healthy subjects with normal hearing.

Methods

We used the Feyts caloric test to stimulate the vestibular system [14]. This test is performed with the subject in seated position. During irrigation of the external auditory meatus (10 mℓ at +20°C for 10 s), the subject's head is tilted 30° forward and the lateral semicircular canals are in the horizontal plane. When instructed by the physician 60 s after the start of irrigation, the subject quickly throws his head back 90°. In order to standardize the conditions, unlike the original method of Feyts, the subject throws his head back on a headrest. This reduces to a minimum the possible influence of additional factors (tension of cervical muscles, contrived position of the head, etc.). In the opinion of Ye. M. Tsirul'nikov [15], the Feyts test is similar to the "otolith reaction" (OR) test of Voyachek. Indeed, both tests involve combined stimulation: concurrently with a cupuloendolymphatic shift there is displacement of otoliths. However, the resemblance is far from complete, since receptors of only one of the lateral canals are stimulated in the Feyts test, while a shift of endolymph occurs only after orientation of the head is changed and simultaneously with displacement of otoliths, i.e., processes occurring in the labyrinth are not as complex as in the OR. Let us note that in the Feyts test irrigation is brief and the pseudoacoustic effect of the stream of liquid is minimal (because of the 1-min pause after irrigation). The same pause can be used to dry the auditory meatus. The Feyts test is well-tolerated, since autonomic reactions are seldom observed and there are virtually no sensory reactions.

For electronystagmography, we used a standard ink-tracing electroencephalograph, cutaneous electrodes were situated at the lateral canthi of the eyes. Along with nystagmus, other channels of the instrument were used to record the time of delivery and intensity of audio signals, as well as mark of perception of the audio signal by the subject. Electronystagmograms were processed by hand. We estimated the following nystagmometric characteristics: latency period, duration of nystagmus, mean amplitude, mean frequency and mean velocity of slow component (SCV) on a 10-s segment corresponding to culmination of nystagmus. We used the method of V. G. Bazarov [16] to measure SCV.

Thresholds of bone conduction were determined using a standard AP-02 audiometer, changing the intensity of the audio signal at 1 dB intervals. The audio signals (250 to 2000 Hz) lasting about 0.5 s were delivered at irregular intervals, ranging from 1 to 8 s. The subject was in a sound-proof chamber with twilight lighting. At first, we determined his base hearing, calculating the mean threshold from the results of 9-12 readings. Right after he threw his head back, we again measured the auditory thresholds and took such readings regularly for 20-30 min (usually it was possible to take 45-50 or more readings in this time). It is known that there may be individual physiological fluctuations of hearing threshold, which are not caused by overt exogenous factors, in the range of up to 5 dB. For this reason, only changes constituting at least 5 dB were considered noteworthy. A single test lasting 1 min at the same frequency of audio signal was called an experiment. In all cases, the tests were made in the mornings. Most of the subjects were submitted to repeated tests (2 to 8 times), depending on the particular objective of a given series of experiments. For example, we tested 1 ear of 11 subjects twice (using a 250 Hz signal the first time and 2000 Hz the second), and 23 underwent 4 tests (measuring thresholds for each ear with two acoustic signals), etc.

This study was conducted on 60 subjects (234 tests) 17-45 years of age, with normal hearing and without vestibular disturbances.

We used nonparametric statistical criteria (criterion of Wilcoxson, sign criterion, χ^2) to assess the results.

Results and Discussion

Vestibular Reactions

Nystagmus was not present in each experiment: the Feyts test did not elicit nystagmus in some subjects (15 out of 60). As a rule, nystagmus appeared upon the first stimulation, and then it was observed in all of the tests. If, however, nystagmus was not present in the first test, we usually were unable to demonstrate it in the others. The Feyts test yielded dissimilar results in only three subjects, i.e., in some tests nystagmus was absent and in others it was present. The qualitative similarity of responses of most subjects tested repeatedly indicates that the Feyts test does not leave lasting residual functional changes in the vestibular system. In view of the fact that the Feyts test is used relatively seldom in practice, we are submitting the results of statistical processing of nystagmometric characteristics obtained from analysis of 104 electronystagmograms on 45 subjects (see Table). Since no nystagmus was observed in some cases, these data should be interpreted as approximating the average "norm" for this test. It is opportune to mention here that the absence of nystagmus with the Feyts test is not a sign of pathology. The mean values of nystagmometric characteristics do not differ very much from those described for the "norm" with other caloric test methods [17-19]. The only exception is the latency period: with the Feyts test, nystagmus appears only after there is a change in orientation of the semicircular canal and, consequently, the latency period is, so to speak, artificially extended by 60 s.

Hearing

There was a rather significant probability of change in hearing threshold under the influence of vestibular stimulation: the thresholds changed in 48 out of 60 subjects (P<0.01; summarized results). The decline of thresholds (i.e., improvement of hearing) occurred reliably more often under the influence of caloric stimulation than worsening (P<0.01). Repeated tests under the same conditions on the same subjects revealed that the direction of change in threshold is individual and a rather stable feature in the subject. We encountered virtually no instances of noncoinciding direction of changes in hearing thresholds in repeated tests. Exceptions from this rule were random in nature. Evaluation was made by the nonparametric criterion of Wilcoxson with confidence probability P = 0.01. A subject's individual capacity to react with a decline or, on the contrary, rise of thresholds persisted with both acoustic stimuli we used.

Nystagmometric characteristics (%) with use of the Feyts test

Parameter	M	σ	m
Latency period, s	63,8	3,0	0,6
Duration of nystagmus, s	108,0	31,2	6,2
Frequency, Hz	1,48	0,3	0,09
Slow component amplitude, degrees	8,3	5,1	1,0
Slow component velocity, degrees/s	16,3	5,2	1,0

There were changes in hearing thresholds both in cases where the vestibular stimulus was associated with nystagmus (45 subjects) and without nystagmus (15); however, the effect of caloric stimulation on hearing cannot be considered independent of the reaction of the vestibular system. The probability of a change in hearing threshold was substantially greater in cases where nystagmus was observed (41 subjects) than without it (7 subjects).

The changes in hearing thresholds of different subjects differed not only in direction, but absolute value. For the category of subjects who responded with a decline of threshold, the maximum change constituted 20 dB, while the averaged result constituted 7.3±3.0 dB. The maximum change in threshold for subjects who reacted with elevation of threshold constituted 15 dB and the mean result was 8.3±2.1. We were unable to demonstrate a correlation between the value by which hearing threshold changed and intensity of nystagmus: a distinct change in threshold could be detected not only with nystagmus having a high SCV, but with mild reaction and even in the absence of nystagmus.

In the tests with contralateral vestibular stimulation. the individual changes in hearing thresholds presented the same qualitative features as with homolateral stimulation. In other words, both the direction of change in threshold and degree of change were unrelated to direction of nystagmus.

In the vast majority of cases (42 out of 48), the hearing threshold changed within the very first seconds after throwing the head back. The change rapidly reached a maximum level, then there was restoration of base threshold level within 30 min. Such changes in threshold sensitivity may be considered typical of individuals who reacted by both a decline and elevation of threshold. Less

Often, we observed undulant change in hearing thresholds, in which case the recovery of base level did not occur smoothly; rather it was associated with another 2-3 deviations that did not reach the maximum value. In some cases, restoration of thresholds took over 1 h.

As a control, we additionally measured hearing thresholds of some subjects after throwing the head back without prior irrigation of the auditory meatus (8 subjects), as well as with irrigation without subsequent change in position of the head (8 subjects). No changes in auditory sensibility were demonstrated in these experiments.

We failed to demonstrate any specific distinctions in the changes in hearing thresholds that were found in this study, which could be attributed to the nature of vestibular afferentation. Thus, with the same vestibular stimulus some subjects presented a decline of threshold of bone conduction and others a rise; with change in direction of nystagmus (tests with contralateral stimulation), we did not observe qualitative change in the results. Finally, the degree of change in threshold was not related to intensity of the vestibular reaction.

It must be specially stressed that the nature of change in hearing thresholds (i.e., improvement or worsening of hearing) was an individual trait of a subject. The threshold changes were quite persistent, lasting for a long time, and they exceeded substantially (by tens of times) the duration of the vestibular reaction. The changes in hearing were referable to both ears to the same extent, and to perception thresholds of both low-frequency (250 Hz) and high-frequency (2000 Hz) signals, i.e., they were, so to speak, universal.

Our findings must be taken into consideration when conducting vestibulometric examinations, if they directly precede audiological tests, since the results of the latter could be substantially altered in such a case.

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POSSIBLE IMPAIRMENT OF RESPIRATORY REGULATION UNDER HYPERBARIC NITROGEN NARCOSIS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 24 Jul 81) pp 59-61

[Article by L. A. Bryantseva, A. V. Suvorov and I. S. Breslav]

[English abstract from source] In order to explore the possibility of disorders in the respiration regulation under conditions of hyperbaric nitrogen narcosis, experiments on 4 test subjects were carried out. Nitrogen narcosis was simulated by nitrous oxide. The ventilation increment was measured as a function of an increase of the hypercapnic stimulus. A combination of high degrees of hypercapnia and the narcotic effect may lead to ventilation inhibition and respiration disturbance.

[Text] The narcotic effect due to high partial nitrogen pressure is one of the deleterious factors, to which man is exposed in deep dives with the use of nitrogen and oxygen breathing mixtures.

Does this effect extent to the nerve centers that control respiration? Investigation of this matter is considered particularly important, since the respiratory system carries an increased load when the gas environment has a high density and, at the same time, it should maintain adequate lung ventilation, which is needed for normal supply of oxygen to the body and elimination of carbon dioxide. This load is particularly great during physical work and with high CO_2 content of inhaled gas.

There is information in the literature concerning depression of efferent activity of the respiratory center in cats in a nitrogen-oxygen atmosphere at a pressure of 11 kgf/cm² or more [1]. At the same time, some researchers [2] believe that respiratory disturbances in man under hyperbaric conditions, including a diminished reaction to CO_2, are attributable to the higher density of the atmosphere.

In studying this question, we deemed it expedient to determine the narcotic effect of a neutral gas, uncomplicated by any influence of gas density and viscosity, on mechanics of respiration, i.e., to conduct studies at normal atmospheric pressure on the model of hyperbaric nitrogen narcosis. The narcotic effect of nitrous oxide is a recognized model of hyperbaric nitrogen narcosis

[3-5]. For this reason, our objective here was to determine the effect of inhalation of nitrous oxide on regulation of respiration. We used a popular method for this purpose: measurement of reaction of pulmonary ventilation on progressive build-up of a hypercapnic stimulus.

Methods

A total of 4 subjects (27-37-year old men) participated in these studies. We conducted 5-7 tests of ventilation reaction to hypercapnia on each of them, using a gas mixture for breathing consisting of 67-75% oxygen and 25-33% nitrous oxide or nitrogen (in the control). The tests were performed in the 105th-120th min of breathing with one of these gas mixtures.

We used the rebreathing method [6]. The subjects breathed through the mouthpiece of a 13-ℓ spyrograph filled with a gas mixture of the following composition: CO_2 7%, nitrous oxide or nitrogen 25-33%, O_2 60-68%. Alveolar CO_2 tension (p_ACO_2) was recorded on a Beckman B-12 capnograph and pulmonary ventilation ($\dot{V}_E$) on the spyrograph for 3-s intervals. Rebreathing usually lasted 2-5 min; p_ACO_2 in the system reached a mean of 65 mm Hg by the end of the test.

We determined the $\dot{V}_E$ increment per mm Hg, increase of p_ACO_2 (parameter S--inclination of line of regression $\Delta\dot{V}_E/\Delta p_ACO_2$) and difference between values of this parameter obtained when using gas mixtures with nitrous oxide and nitrogen. All of the calculations were made on ANG-2200b and WANG-2200b computers.

Results and Discussion

Overall evaluation of respiratory reactions to hypercapnia, on the basis of comparing the values of parameter S derived for the entire set of values for p_ACO_2 and $\dot{V}_E$ obtained during the tests, failed to demonstrate a significant effect from inhalation of nitrous oxide. True, in most cases the mean increment of pulmonary ventilation when using the mixture with nitrous oxide was lower than in the control, but these differences did not reach a level of statistical significance (see Table).

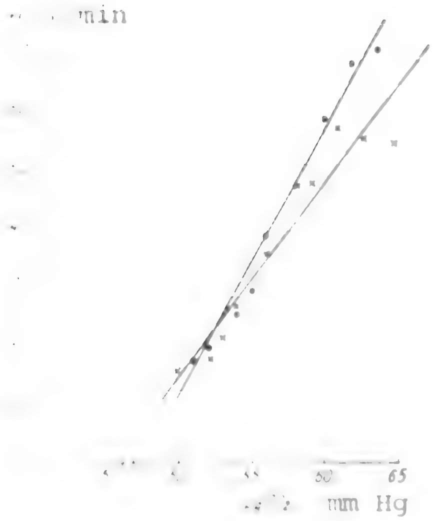
At the same time, examination of ventilation during rebreathing of mixture with nitrous oxide revealed the following distinction: while the build-up of $\dot{V}_E$ proceeded in about the same manner as in control tests at up to 55-60 mm Hg p_ACO_2, with further intensification of the hypercapnic stimulus increase of $\dot{V}_E$ slowed down or stopped, occasionally changing to a decline of this parameter (see figure). This phenomenon was consistently demonstrated in three subjects and absent in one. The verbal accounts of the subjects conformed to these findings; they reported deepening of the narcotic state (clouded consciousness at the end of the rebreathing period).

On the basis of this finding, we calculated the increment of pulmonary ventilation in the final period of rebreathing, corresponding to a p_ACO_2 range of 58 to 65 mm Hg. We found that this parameter was reliably lower in three subjects when inhaling a gas mixture with nitrous oxide than in the tests where nitrogen was used (see Table).

Pulmonary ventilation reaction to progressive hypercapnia (S, ℓ/min/mm Hg p_ACO_2) when breathing with mixtures of oxygen with nitrogen and nitrous oxide (M±m)

Subject	Pulmonary ventilation					
	for entire range of p_ACO_2 increase			for p_ACO_2 in the range of 58-65 mm Hg		
	nitrogen	nitrous oxide	differences	nitrogen	nitrous oxide	differences
A. S.	2,6±0,5	1,8±0,4	−0,8±0,4	3,3±0,8	0±0,3	−3,3**±0,7
A. M.	1,3±0,2	1,0±0,1	−0,3±0,2	1,4±0,2	1,2±0,2	−0,2±0,3
S. S.	2,0±0,2	1,7±0,1	−0,3±0,3	2,0±0,9	0,2±0,4	−1,8*±0,7
S. R.	2,0±0,2	2,1±0,1	+0,1±0,2	2,6±0,1	0,2±0,7	−2,4*±0,6

$*P<0.05$ $**P<0.01$



Example of reactions of pulmonary ventilation on progressive hypercapnia in subject A. S. The dots refer to value of $\dot{V}_E$ with inhalation of nitrogen-oxygen mixture and crosses to its value with inhalation of mixture of oxygen and nitrous oxide

a, b) corresponding lines of regression ($\dot{V}_E/p_ACO_2$)

Thus, as a result of our study of the averaged reaction to hypercapnia, it was established that nitrous oxide narcosis does not affect regulation of respiration. A substantial distinction is obscured with the use of this traditional method: the potentiating effect of hypercapnia itself on degree of narcotic effect [7]. In this case, it was necessary to make a differentiated analysis of the dynamics of ventilation reaction to rise of p_{CO_2}. The results of such analysis revealed that the effect of narcosis with nitrous oxide on the system of regulation of respiration, which is insignificant in normocapnia and moderate hypercapnia, may be more significant with extreme degrees of hypercapnia, and it leads to depression of ventilation.

This pattern, which was demonstrated for the effect of nitrous oxide, is probably also applicable to the narcotic effect of nitrogen at high pressure. According to some data, the narcotic effects of nitrogen and nitrous oxide, measured on the basis of their influence on the results of psychophysiological tests, are in a ratio of 1:30 or 1:50 [3]. Consequently, the breathing mixtures used, which contained an average of about 30% nitrous oxide at normal atmospheric pressure, are approximately equivalent in narcotic effect to a normoxic nitrogen-oxygen mixture at a pressure of at least 9 kgf/cm^2 ("depth" of about 90 m), and at such pressures nitrogen narcosis does indeed occur.

It should be borne in mind that increased density of a hyperbaric environment, which makes breathing difficult (mainly during intensive physical work [7-10]), is a predisposing factor for CO_2 retention [11] which, in turn, can deepen the narcotic effect. Under such conditions, one cannot rule out the possibility of development of a vicious circle--breathing difficulty-hypercapnia-deeper nitorgen narcosis-depression of breathing--which could lead to decompensation of respiratory function.

On the basis of our findings, we can make the following conclusion: the combination of narcotic effect and extreme hypercapnia can impair regulation of respiration and depress ventilation. For this reason, it is imperative to institute preventive measures to avoid hypercapnia in an individual working at high ambient partial nitrogen pressure.

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MITOTIC ACTIVITY AND VOLUME OF EPITHELIAL CELL NUCLEI OF RAT CORNEA FOLLOWING SPACEFLIGHTS IN BIOSATELLITES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 21 May 81) pp 61-66

[Article by I. V. [illegible] (deceased), [illegible] Rudneva, N. G. Sepeteva and [illegible] V. Yankova]

[English abstract from source] On total preparations of the cornea of rats flown on Cosmos-936 and Cosmos-1129 the following parameters of the epithelial tissue were studied: mitotic index, ratio of mitotic phases, number of abnormalities of cell division, and number of chromosome aberrations in anaphases. These parameters were considered to be indicators of physiological regeneration. The nuclear volume of cells of two inner epithelial layers was measured, using a modified karyometric technique that yielded representative data. The lack of significant changes in the above mitotic parameters can be attributed either to the absence of a strong stress-reaction of rats postflight or to the discrepancy between the time of animal sacrifice and the time of the maximum post-stressor inhibition of mitotic activity. This study revealed some data suggesting that in weightlessness the rate of cell division remained unaltered. The mean nuclear volumes of corneal epithelial cells changed significantly (P<0.01) at the examination stages (days 6 and 29). This may be associated with rearrangements in the regulatory systems of the animal body postflight. It cannot be ruled out that an increased cell activity measured with respect to the nuclear size correlates with the intraocular pressure.

[Text] Homeostasis of rapidly renewed tissues is maintained in the body by processes of physiological regeneration. This process is determined by many parameters: proliferative pool--number of cells in the mitotic cycle, tissue life span, rate of renewal and mitotic activity (MA).

MA, as assessed by the mitotic index (MI), is the best studied criterion of regeneration. The amount of information referable to the study of MA is increasing constantly. Studies have been made of daily, seasonal and age-related fluctuations of MA [1, 2]; it has been determined that there is a cell division reaction to various conditions and agents, including stressors

[3]. Virtually no studies have been made of the distinctions of effects of spaceflight factors on the process of physiological regeneration. Laboratory experiments revealed a decline of bone marrow and liver MA in animals submitted to accelerations and vibration [4-6]. This information is indicative of the need to investigate physiological regeneration in animals exposed to weightlessness.

This article deals with the results of studies of mitosis and karyometry of corneal epithelium of rats flown aboard Cosmos-936 and Cosmos-1129 biosatellites.

Methods

We studied MA, correlation between mitotic phases, number of impaired cell divisions* and chromosome aberrations in the corneal epithelium of male Wistar rats, clone SPF. After sacrificing the animals, the enucleated eyes were fixed in Bouin fluid. Total corneal preparations were made using an original technique [8], and they were stained with hematoxylin according to Caracci. We examined at least 100 fields of vision (ocular 7×, obj. 60×) in each cornea, in the middle and over the edges; MI was expressed per thousand. We counted the cells by means of a special diaphragm which circumscribed a 2500 μm^2 segment of the field. In order to determine the proportion of mitotic phases, mitotic pathology and chromosome aberrations, we counted at least 600 dividing cells in anaphase in each rat.

Karyometry was performed, using an RA-6 projection attachment ["drawing apparatus"] at a magnification of 2000× to draw the outlines of nuclei of at least 100 interphase cells from two internal epithelial layers of each cornea. The results of measuring the volume of nuclei in rats flown aboard Cosmos-936 revealed that 100 nuclei are enough to obtain statistically reliable data, so that in the second instance, we drafted 50 cell nuclei from each cornea. With this number of readings, the mean volumes of cell nuclei from the right and left cornea did not differ in 45% of the cases, differed by 5-9% in 40% of the cases and by 10-14% in only 15% of the cases. The large and small diameters of projections of the nuclei were measured by means of a special two-axis ruler [9]. We determined the value of the class in logarithms using the table in [10], to which the measured nuclei belonged; subsequent calculations were made by the usual methods [11]. The groups and quantity of animals examined are listed in Table 1.

Results and Discussion

We demonstrated 32.1±0.84 to 36.4±1.07 cells over an area of 2500 μm^2 in the cornea of all examined rats; the differences did not exceed the statistically permissible range with the calculation method we used. Epithelial cells of the cornea are renewed in 6.9 days in rats [12]; consequently, for the duration of the flight there were at least two successive cell generations. The absence of changes in number of cells immediately after the flight shows that there was apparently no change in intensity of cell reproduction in weightlessness. There are contradictory data, which were obtained from studies of various biological objects (bacteria, algae, infusoria, etc.), concerning the rate of cell reproduction in weightlessness.

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*Many cytologists use the concept of "mitotic regimen" [mode] to refer to the sum of these parameters.

Talbe 1. Groups and quantity of rats examined

Index and characteristics of groups	Number of animals	
	Cosmos-936	Cosmos-1129
C_0--vivarium control (preflight)	0	5/4
C_1--vivarium control (0-6 h after flight)	5/5	0
C_2--same (5-11 h after flight)	5/5	7/6
C_3--same (26 days after flight)	0/4	5/5
M_0--model experiment (before flight)	0	5/4
M_2--same (5-11 h after flight)	5.5	7/6
M_3--same (29 days after flight)	0	5/5
W_1--experiment (0-6 h after flight)	6/6	0
W_2--(5-11 h after flight)	5/4	7/7
W_6--experiment (6 days after flight)	0	7/5
W_{29}--experiment (29 days after flight)	0/3	5/5
Cf_1--artificial gravity [centrifuge] (0-6 h after flight), 1 day	4/4	0

Note: In parenthesis is time at which animals were sacrificed. Numerator--animals examined to determine mitotic regimen, denominator--for karyometry.

Table 2 lists the results of cytological examination of corneal epithelium of rats flown aboard Cosmos-936. The mean values of MI virtually coincided in the control groups (±9%, P>0.02), whereas in the experimental groups they did not differ from the control (P>0.05), although they were up to 20% higher in the W_1 and CF_1 groups. The correlation between postflight mitotic phases fluctuated in the range of control values.

Table 2. Mitotic regimen and volume of epithelial cell nculei from cornea of rats flown aboard Cosmos-936 biosatellite

Rat group	MI	Correlation betw. mitotic phases		Pathological mitoses, %			Volume of nuclei, log
		M+P/A+T	M/P	$M \pm m$	multi-polar	retard. chromosomes	
C_1	8,2±0,47	5,1±0,72	1,2±0,21	14,5±1,45	0,8±0,21	0,7±0,18	1,8845±0,00519
C_2	8,5±0,41	4,0±0,62	1,7±0,18	13,7±1,73	0,7±0,16	1,0±0,14	1,8980±0,00514
M_2	9,0±0,[illegible]	2,8±0,85	1,3±0,23	10,5±0,95	0,6±0,13	1,0±0,18	1,9000±0,00526
W_1	9,5±0,52	3,6±0,40	1,1±0,11	9,5±1,45	0,4±0,08	1,1±0,31	1,8950±0,00351
W_2	8,7±0,50	4,4±0,81	2,0±0,49	14,0±0,88	0,5±0,16	0,8±0,20	1,9040±0,00405
Cf_1	10,4±0,63	4,4±0,74	1,4±0,25	9,7±1,51	0,7±0,18	0,5±0,15	1,9080±0,00461

Note: Mean data for groups are listed.
Key: P) prophase M) metaphase A) anaphase T) telophase

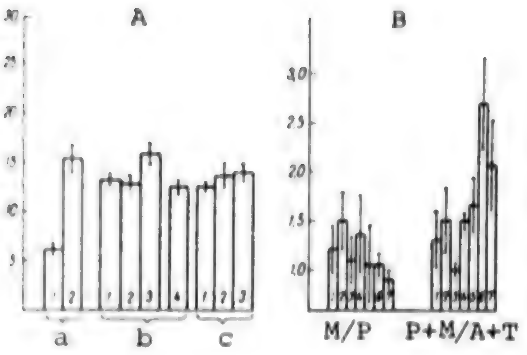

Figure 1.
Criteria of mitosis in rat's corneal epithelium. X-axis, group of rats.

- A) mitotic index (MI, per thousand) in epithelial cells of rat cornea
  - a) preflight data
  - b) after 5-11 h and 6 days
  - c) after 29 days
  - 1) vivarium control
  - 2) model experiments
  - 3) experiment immediately after flight
  - 4) experiment 6 days after flight
- B) Correlation between mitotic phases in rat corneal epithelium
  - 1,3) vivarium controls
  - 2,4) model experiments
  - 5,6,7) experiments after 5-11 h, 6 and 29 days, respectively

The number of cell division anomalies varied over the same range in the control and experiment; pathological mitoses were represented mainly by retention of chromosomes in metakinesis (see Table 2). Chromosome aberrations were encountered in 0.5-1.1% of the anaphases.

Figure 1 illustrates the main parameters of mitosis in the corneal epithelium of rats flown aboard Cosmos-1129. We see that there was no appreciable difference between rats in the control and model experiment groups with regard to value of MI. The only exception were the Co group of animals, in whom MI was one-half the value of rats in other groups. In the experiment, only the W_2 group of animals presented an appreciable increase of MI, as compared to the C_2 group ($P<0.02$) and M_2 ($P<0.05$). The other parameters were the same in the control and experiment, with the exception of the W_6 group, in which we demonstrated an appreciable increase in ratio of first mitotic phases to the sum of anaphases and telophases (2.7±0.66, versus the maximum of 1.6±0.28 in the control, 2.1±0.56 in the W_{29} group). The increase in quantity of early mitotic phases in this group of animals is apparently the consequence of a stress reaction, similar to the one described in the rat cornea after electric stimulation [13].

Morphological and histochemical studies revealed a distinct stress reaction in rats after spaceflights, including the one aboard Cosmos-936 [13, 14]. Rats flown aboard Cosmos-1129 biosatellite also presented moderate signs of stress reactions [15]. It is known that stress elicits depression of MA of renewing tissues [3, 16]. The absence of this effect in the described experiments can be interpreted in different ways: either the stress reaction was not sufficient to disrupt the rate of cell division, or the time at which the animals were sacrificed did not coincide with the time of MA depression. The latter is more probable, since a decline of MA was not observed in the W_6 group of rats who were submitted to recurrent immobilization stress after the flight. These animals merely presented a change in mitotic phase ratio.

Karyometric studies revealed that the size of cell nuclei, which is a constant parameter for a given cell population, reacts rapidly to exogenous factors or a change in "status" of tissue [10, 17]. It was proven that the nucleus volume, which is a function of many factors (ploidy, ineness [or degree of dispersion] of proteins, etc.), is determined when these conditions are equal primarily by functional activity of cells [10, 18].

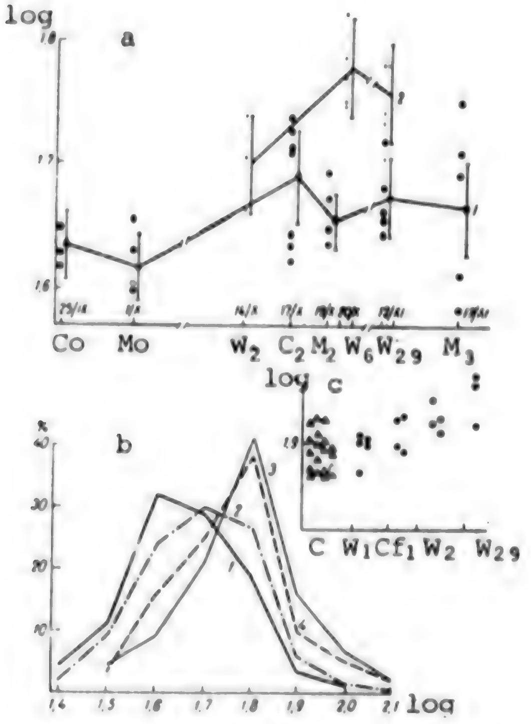

Figure 2.

Results of karyometry of rat's corneal epithelium

a) logarithms of mean volumes of epithelial cell nuclei in different rats and weighted means of groups (Cosmos-1129). Y-axis, logarithms; x-axis, groups and dates animals were sacrificed

b) variational curves of logarithms of nuclear volumes--weighted means for groups. Y-axis, percentage of nuclei of given class; x-axis, logarithms.
  1) weighted mean for all tested rats in C and M groups
  2) W_2 group
  3) W_6 group   4) W_{29} group

c) logarithms of mean nuclear volumes (Cosmos-936). Y-axis, logarithms; x-axis, groups of animals examined. C--animals in model experiment and controls

Table 2 lists the logarithms of mean volume of cell nuclei of corneal epithelium in the experimental groups of animals flown in Cosmos-936. The differences are statistically insignificant. In the control and model experiment the mean volumes of corneal cell nuclei fluctuated in different animals from 1.8710±0.01260 to 1.9210±0.01070 log ($P>0.02$); in the experiment the differences between extremes, 1.8530±0.0130 and 1.9320±0.0078, were statistically significant ($P>0.001$).* The rats in the W_2 group had the largest nuclear volumes.

The data obtained from karyometry of the corneal epithelium of rats flown aboard Cosmos-1129 are illustrated in Figure 2. The curves illustrated in Figure 2a were plotted with consideration of time parameters. This figure shows that the logarithms of mean cell nucleus volumes were within the statistically permissible range of fluctuations in rats of the control group and model experiment sacrificed at different times over a 60-day period. In the experimental groups, there was distinct increase in volume of cell nuclei, and it was statistically significant in the W_6 and W_{29} groups. The nuclei were also larger than in the control in some of the rats sacrificed 6-11 h after the flight (see Figure 2, Table 3).
The increase in mean volume of cell nuclei of corneal epithelium of rats occurred due to a shift of variation curves in the direction of higher numbers with a corresponding two-class shift of mode of nuclear volume (see Figure 2b). In the control, 73.3% of the rats have a modal class of cells whose nuclear volume falls into the class with a value of

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*In karyometry, when the number of measurements is large, differences with $t \geqslant 3.7$ and $P<0.001$ are generally considered statistically reliable [10].

Table 3.
Distribution of animals according to value of modal class of nucleus volume in corneal epithelial cells of rats from experiment aboard Cosmos-1129

Value of modal class	Animal group examined								
	Co	Mo	C_2	C_3	M_2	M_3	W_2	W_6	W_{29}
1.6	4	4	2	5	5	2	2	0	0
1.7	0	0	3	0	1	2	3	0	1
1.8	0	0	1	0	0	1	2	5	4
n	4	4	6	5	6	5	7	5	5

1.6 log, 20%--1.7 and only 6.7% of the cases (2 out of 30 tested rats) presented a value of 1.8 log for the modal class. In the experiment, most animals were referable to the class of 1.8 log for this feature. Table 3 shows the distribution of rats according to mode of volume of cell nuclei from the corneal epithelium.

Having detected the enlargement of corneal cell nuclei in rats after flight aboard Cosmos-1129, we made a more thorough analysis of the data obtained from the preceding experiment. We additionally measured the corneal cell nuclei of 7 rats: 4 control (C_3 group, see Table 1) and 3 experimental (W_{29} group). Two control rats and all of the experimental ones underwent bilateral labyrinthectomy before starting the experiment [19]. All of the rats were sacrificed 29 days after termination of the experiment. The mean size of corneal cell nuclei of all examined rats is shown in Figure 2c. Against a background of minor fluctuations in mean volume of nuclei of the corneal epithelium in control groups and model experiment rats which were put together and designated by C, we see that the W_2 group animals and particularly those in W_{29} presented larger nuclei than most animals in the C group. There were changes similar to those illustrated in curve 2, a.

It is quite difficult to explain the demonstrated persistent enlargement of cell nuclei in the internal layers of corneal epithelium from rats flown in biosatellites, particularly since this phenomenon persisted when the animals presented good morphological and physiological signs at the late postflight stages. The karyometric data were obtained from examination of adrenal cells, hypothalamic neurocytes and thyroid C cells, i.e., endocrine cells which bear a direct functional load during flight. At the early postflight stage, the size of nuclei of the above-mentioned cells undergo changes in different directions, which conform with morphological signs of changes in functional activity of the organs [20-22]. At the late postflight stages there is normalization of organ morphology (including the volume of cell nuclei).

The corneal epithelium performs a protective function and, together with connective tissue membranes, apparently carries a physical load. This is indicated by the presence of highly developed cytoskeletal structures (for example, a rich network of tonofibrils) in epithelial cells. The experimental data enable us to rule out an increase in ploidy and dispersion of cell proteins as causes of increase in nuclear volume. Perhaps, the demonstrated phenomenon, which is an indicator of functional activity of cells, is attributable to a change in regulatory systems of the organism under the extreme conditions of spaceflights. Perhaps, there is a correlation between the size of corneal epithelial cell nuclei and intraocular pressure. However, we found no indications of such a link in the available literature.

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CATECHOLAMINES AND ENZYMES OF THEIR METABOLISM IN RAT MYOCARDIUM AFTER FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 18 Aug 80) pp 66-68

[Article by R. Kwetnianski, R. A. Tigranyan and T. Torda (CSSR and USSR)]

[English abstract from source] In the myocardium of the weightless and centrifuged rats flown for 18.5 days onboard the biosatellite Cosmos-936 the catecholamine concentration and activity of enzymes involved in their synthesis and degradation--dopamine-β-hydroxylase, monoamine oxidase and catechol-O-methyl transferase--were measured. The catecholamine concentration in the myocardium of both flight groups significantly increased, and the enzyme activity did not change. These results suggest that an exposure to space flight increases the catecholamine concentration and exerts no effect on their synthesis and degradation in the rat myocardium.

[Text] Studies have shown that acute immobilization stress causes a decrease in catecholamine (CA) content of the rat myocardium; however, repeated use of immobilization (repeated stress) does not elicit such an effect. The stability of CA concentration in the myocardium of rats submitted to recurrent stress is most probably the result of increased synthesis of CA, since the activity of enzymes of CA synthesis in the heart of these animals also increased (data of R. Kwetnianski). On this basis, we assumed that we could expect either a decline of CA content of the myocardium as a manifestation of acute stress, or that there would be no change in level thereof as a manifestation of the lack of stressogenicity of spaceflight or the animals adaptation to flight, in rats flown aboard Cosmos-782 biosatellite. It was found that CA content of the rat myocardium increased significantly after the flight, and the elevated CA level was unrelated to change in synthesis or degradation of CA in the myocardium, as indicated by the unchanged level of activity of enzymes involved in CA synthesis and degradation [1].

Our objective here was to assay CA and enzymes of their metabolism in the rat myocardium after a flight aboard the Cosmos-936 biosatellite, as well as to compare these data to the results of prior studies aboard Cosmos-782 and, on this basis, to assess the stressogenicity of prolonged weightlessness.

Methods

The studies were conducted on male Wistar-SPF colony rats flown for 18.5 days in space aboard the Cosmos-936 biosatellite.

The myocardium was excised immediately after decapitating the animals the pericardium, remnants of large blood vessels and adipose tissue were rapidly removed; it was weighed and immediately frozen in liquid nitrogen, then stored in frozen form until the start of treatment. The heart was homogenized in 0.25 M saccharose so that 100 μℓ homogenate would contain 16 mg tissue. We diluted 50 μℓ saccharose homogenate in 0.1 N $HClO_4$ so that 25 μℓ of homogenate would contain 0.7 mg tissue; the homogenate was centrifuged under refrigeration for 10 min, at 10,000 G, and CA concentration in the supernatant was determined [2]. This method was used to assay total epinephrine (E) and norepinephrine (NE) content (since the heart contains mainly NE, the obtained data are listed only as NE concentration). We measured the activity of dopamine-β-hydroxylase (DBH) [3] and monoamine oxidase (MAO) [4] in the initial saccharose homogenate; we determined the activity of catechol-0-methyl transferase (COMT) [5] in the supernatant (10,000 G).

Results and Discussion

NE concentration in the myocardium of FW_1 and FC_1 groups of rats increased considerably immediately after landing, as compared to the vivarium control; however, this increase was unreliable in comparison to synchronous control rats (SW_1 and SC_1). It should be noted that NE content of the myocardium of both groups of rats in the synchronous control groups did not differ reliably from the levels in the vivarium control. NE concentration in the myocardium of both flight groups (FW_3 and FC_2) did not differ from control rats 25 days after landing (Figure 1).

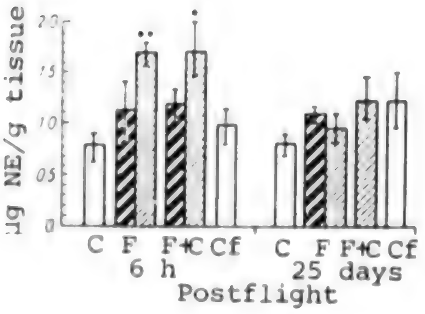

Figure 1.
NE concentration in rat myocardium. Here and in Figures 2 and 3, from left to right, columns refer to following groups of animals: VC_1 [vivarium control], SW_1 [synchronous control experiment, weightlessness], FW_1 [flight group, weightlessness], SC_1 [synchronous, centrifuge], FC_1 [flight group, centrifuge], C^0_1 [centrifuge], VC_3, CW_3, FW_3, FC_2 and C^0_2. There were 5 animals in each group. Reliability shown in relation to vivarium control
*$P<0.05$ **$P<0.001$

DBH activity in the heart of flight rats did present some tendency toward increasing, but the changes were unreliable in comparison to parameters of control groups (Figure 2).

COMT activity in the heart of flight animals did not differ from control groups. As for MAO, the level of its activity in the myocardium also showed no change in any of the groups; the only reliable difference was demonstrated 25 days after landing in the flight group, as compared to the synchronous control (Figure 3).

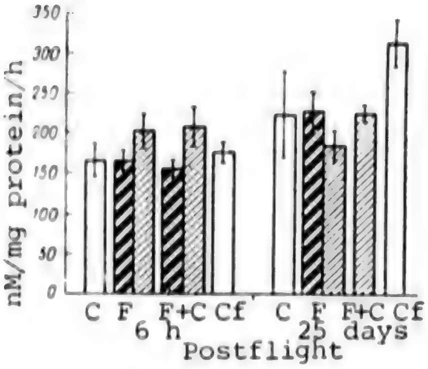

Figure 2.
DBH activity in rat myocardium

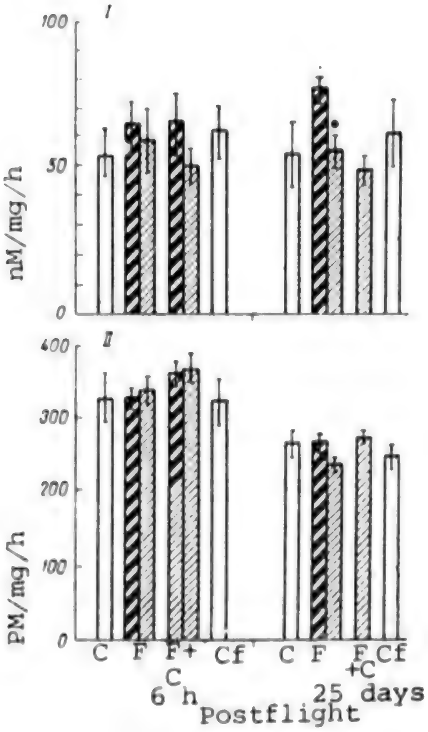

Figure 3.
MAO (I) and COMT (II) activity in rat myocardium. Dot shows P<0.02. Reliability is given in relation to synchronous control

Considering data concerning the effects of acute or recurrent stress on CA content of the heart (data of R. Kwetnianski), we expected that, after assaying CA concentration in the myocardium of flight rats, we would get an answer to the question of the nature of spaceflight stressogenic factor--acute or chronic. We demonstrated a reliable increase in CA concentration in the heart of rats flown aboard Cosmos-782, as compared to control groups [1]. We hoped to obtain this unexpected result again in the experiment aboard Cosmos-936.

Indeed, in rats used in the Cosmos-936 experiment, CA concentration in the myocardium increased significantly in flight rats, as compared to the vivarium control, but the difference was unreliable in comparison to the synchronous [ground-based experiment] control, which was apparently attributable to the small number of animals in the groups; in the Cosmos-782 experiment, the increase in myocardial CA concentration in flight animals was reliable, as compared to both control groups [1]. The increase in cardiac CA concentration in flight animals is not due to the effects of weightlessness, since animals exposed to artificial gravity of 1 G during the flight also showed an increase in CA content. Although there was more reliable increase in myocardial CA concentration in rats submitted to weightlessness and there was less scatter of the data than in rats that were centrifuged in flight, the mean values were the same. For this reason, the cause of increase in CA content of the heart is probably not the prolonged state of weightlessness, but effect of some spaceflight factor that both flight groups were equally exposed to, both during the flight and in the period of landing the biosatellite, since the centrifuge was turned off several hours before landing.

The elevated CA level in the myocardium of flight rats could be attributable, for example, to increased synthesis or decreased degradation thereof. On the basis of absence of change in activity of DBH--an enzyme that synthesizes CA, as well as MAO and COMT, which are enzymes of CA degradation, we assume that the increase in CA concentration did not occur because of altered CA synthesis or breakdown in the heart, but apparently due to increased absorption or diminished secretion of CA. At any rate, the rise in myocardial CA level in rats following a long-term space flight is indicative of a change in myocardial function under spaceflight conditions.

Our findings warrant the assumption that the conditions of long-term spaceflights are not a stressogenic factor for rats.

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UDC: 629.78:612.822.1.015.33

NITROGEN COMPOUND LEVELS IN TISSUES OF RAT CEREBRAL HEMISPHERES AND CEREBELLUM AFTER FLIGHT ABOARD COSMOS-1129 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 5 May 81) pp 68-70

[Article by L. M. Kurkina and R. A. Tigranyan]

[English abstract from source] The content of ammonia, glutamine, urea, glutamic acid, aspartic acid, and GABA was measured to study nitrogen metabolism. Soon after recovery (6-10 hours after recovery) the content of the above compounds in brain tissues increased, except for GABA whose content decreased. Similar but more marked changes were seen in the brain of control rats exposed to a repeated immobilization stress-effect. These changes were still greater in the flight rats exposed to a repeated immobilization stress-effect postflight. It is suggested that the postflight changes of the above parameters of nitrogen metabolism are induced by stress-agents inherent in space flight and recovery.

[Text] Changes were demonstrated in protein metabolism in the rat central nervous system (CNS) during long-term spaceflights in the Cosmos series of biosatellites [1-4], which were attributed to both the effects of weightlessness and various stressors associated with spaceflight.

Our objective here was to study the changes in levels of come nitrogen compounds in tissues of rat cerebral hemispheres and cerebellum after an 18.5-day spaceflight aboard Cosmos-1129 biosatellite, as well as to determine the effects of an additional stressor on the tested compounds.

We assayed, as parameters of nitrogen metabolism, ammonia, glutamine, urea, glutamic acid, aspartic acid and γ-aminobutyric acid (GABA), since these constituents are related to both protein and energy metabolism.

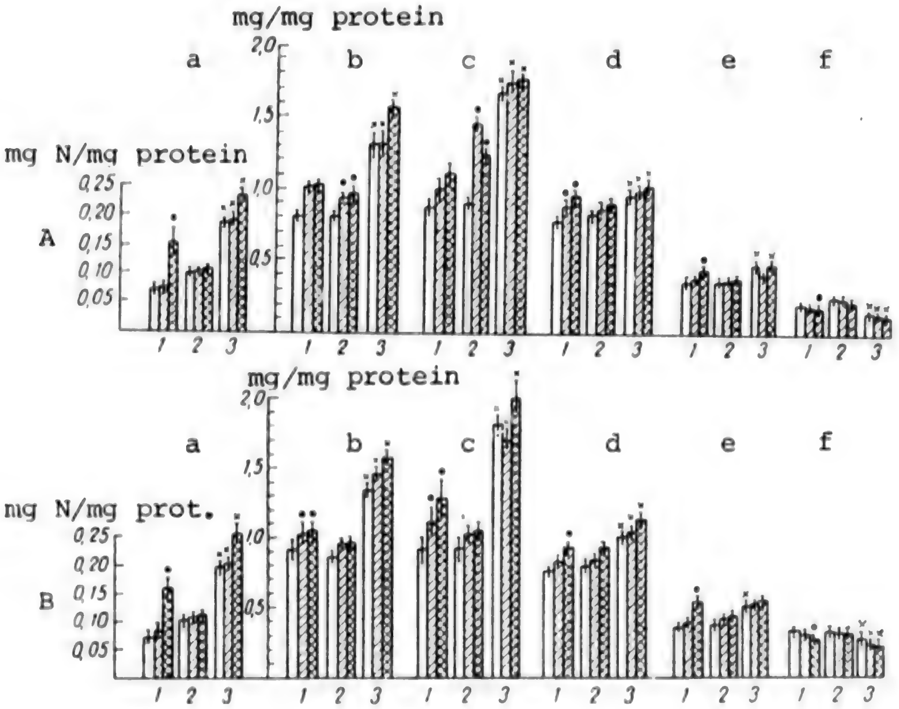
Methods

These studies were conducted on male Wistar-SPF rats (Bratislava, CSSR), flown for 18.5 days in space aboard the Cosmos-1129 biosatellite.

After decapitating the rats, we excised the brain from the skull, isolated its structures and froze them in liquid nitrogen; 5-7 min elapsed from the time of decapitation to freezing. The frozen specimens were stored at a temperature of -40°C for several months. We assayed ammonia [6], glutamine [7], urea [6], as well as free amino acids--aspartic, glutamic and GABA [8], in aqueous-alcohol extracts [5] of tissues from the cerebral hemispheres and cerebellum. We estimated the amounts of all tested substances per unit protein; protein was assayed by the method of Lowry as modified by Bailey [9]. The data were submitted to statistical processing.

Results and Discussion

Immediately after landing, flight rats showed a reliable increase in amounts of ammonia, glutamic, aspartic acids and decrease in GABA of the cerebral hemispheres and cerebellum (see Figure). At the same time, there was slight ($P<0.1$) increase in glutamine and urea content.



Ammonia (a), glutamine (b), urea (c), glutamic acid (d), aspartic acid (e) and GABA (f) content of tissues of rat cerebral hemisphere (A) and cerebellum (B) tissues in experiment conducted aboard Cosmos-1129. White columns--vivarium control; striped and cross-hatched--synchronous experiment and flight. The results (M±m) are given per 5 animals. Statistical reliability: dot refers to $P<0.05$ in relation to vivarium control and ×--$P<0.05$ in relation to corresponding group examined on 6th postflight day (2)

1) 6-10 h after landing
3) 6th postflight day + repeated stress
2) 6th postflight day

Six days after landing, there was a decline in ammonia levels in the cerebral hemispheres and cerebellum (see Figure) of flight rats, and they did not differ from the vivarium control. Glutamine level remained elevated in both the flight rats and those in the synchronous experiment in the hemispheres, and dropped to control levels in the cerebellum. Urea content of brain structures was high in both groups of rats; at this stage of the study, amino acid levels did not differ from control values. These data indicate that an active process of ammonia binding occurs in brain tissue at this stage, and it could be toxic in large quantities and have a deleterious effect on the CNS.

Repeated immobilization stress revealed a drastic increase in ammonia, glutamine, urea, glutamic and aspartic acids, decrease in GABA content of control rats, in both the cerebral hemispheres and cerebellum (see Figure); all these changes were even more marked in the flight group of rats.

In analyzing the findings, it should be noted that the changes in the tested elements of nitrogen metabolism of brain tissue presented the same direction in the hemispheres and cerebellum, but they were more marked in the cerebellum. We were impressed by the fact that the changes in all parameters noted in flight rats immediately after landing were analogous to those demonstrated in vivarium control rats submitted to repeated stress. This could be indicative of the stress-related etiology of postflight changes.

It should be noted that the greater changes in levels of tested compounds, which were demonstrated in flight animals submitted to repeated stress, may be indicative of active adaptation processes and great lability of the nervous system.

Thus, a scrutiny of the data on ammonia, glutamine, urea and tested amino acid levels leads to the conclusion that the demonstrated changes are closely interrelated and that they are indicative of coordinated function of the ammonia-glutamine-glutamic acid-urea system which, on the one hand, provides for rapid detoxification of excess ammonia and, on the other hand, maintains relative stability of GABA content in stress-producing situations.

The virtually complete normalization of levels of the above nitrogen compounds 6 days after landing is indicative of great lability of the CNS and good adaptation thereof to ambient conditions.

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UDC: 628.78:612.014.482.5

MEASUREMENT OF CHARGE AND ENERGY SPECTRA OF HEAVY NUCLEI ABOARD COSMOS-936 ARTIFICIAL EARTH SATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 21 May 81) pp 70-73

[Article* by S. A. Dashin, A. M. Marennyy and G. P. Gertsen]

> [English abstract from source] The measurements were performed using a package of dielectric track detectors mounted behind the shield of 60-80 kg•m^{-2} thick. The charge of nuclei was determined from the complete track length. As a result, 1915 tracks of nuclei with $Z>6$ in the energy range 100-450 MeV/nuclon were detected and identified. The differential charge spectrum of nuclei with $6<Z<28$ and the energy spectrum of nuclei of the iron group were built. For iron nuclei the following ration of isotope groups was obtained: $(Fe^{52} + Fe^{53} + Fe^{54})$:$(Fe^{55} + Fe^{56} + Fe^{57})$:$(Fe^{58} + Fe^{59} + Fe^{60})$ = (0.30±0.08):(0.49±0.10):(0.21±0.05).

[Text] A package of dielectric track detectors (DTD), which is a component of the equipment used in the Soviet-American dosimetric experiment, was installed aboard Cosmos-936, an artificial earth satellite, to take readings related to the heavy component of cosmic rays.

We submit here the results of measuring charge and energy spectra of heavy charged particles, which were obtained by the Soviet participants in this experiment.

Methods

The Cosmos-936 satellite was launched on 3 August 1977. The mission lasted 19.5 days with the following orbital parameters: angle of inclination $i = 62.8°$, maximum distance from earth's surface (apogee) 419 km and minimal distance (perigee) 224 km. The detector package, 100×100×100 mm^3 in size, was inside the satellite in the immediate vicinity of the craft's shell; the plane of the

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*We take this opportunity to express our appreciation to Ye. Ye. Kovalev and V. Ye. Dudkin for giving their constant attention to our work, V. V. Tsetlin for discussing the results, as well as N. A. Bardasheva and L. L. Mironycheva for their assistance in taking measurements.

detectors was parallel to a shell 60 kg•m^{-2} in thickness. The package consisted of 125 layers of KNC cellulose nitrate each 800 μm thick. After termination of the experiment, the detectors were primed [dipped?] in 6 N aqueous solution of NaOH for 5 h at a temperature of 323±0.4°K. Detectors assembled into multilayer units were examined under an optical microscope to determine the maximum primed length (MPL) of heavy charged particle tracks [1]. We determined the particle charge from the measured MPD. MPD as a function of charge Z under these conditions of detector treatment is illustrated in Figure 1. Particle energy at the entry of the package was determined after identification over the entire range in the package.

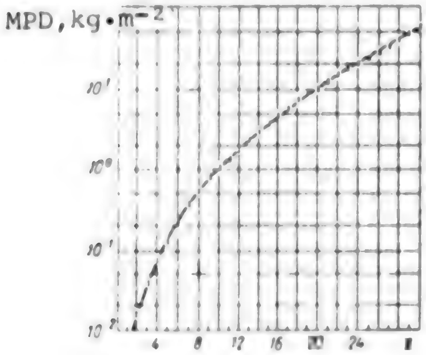

Figure 1.
MPD as a function of particle charge Z

To determine the angular distribution of heavy nuclei under our experimental conditions, we plotted azimuthal distribution and distribution over entrance angles of the particles in the package. From the obtained angular distribution we calculated the efficiency of recording tracks in a layer for plotting spectra as described previously [2]. In analyzing the reading results, we used the methods described in [3] to identify particles, plot spectra and determine isotope composition.

Results and Discussion

To date, we have completed examination of the central part of the package. In plotting the spectra, we took into consideration only tracks contained entirely or partially in the detector layer (16 kg•m^{-2} thick) situated at a depth of 31 kg•m^{-2} from the top surface of the package. We observed in part the tracks contained in the layer beyond its boundaries to measure MPD. In all, we found 1915 tracks with a charge of $Z \geq 6$ which traversed this layer of detectors. The azimuthal distribution according to angles, which was plotted for the most representative group of nuclei (iron groups; Z = 24-28), was virtually isotropic. There was significant deviation from isotropism at angles in excess of 40-50° in the angular distribution for entrance into the package. This was apparently attributable to the increased thickness of shielding material in directions corresponding to angles greater than 50°. Analysis of the directions of entry of particles into the isolated detector layer revealed that no more than 3% of the particles enter through the posterior hemisphere. For this reason, we took into consideration only the tracks of particles that traversed the anterior hemisphere in the entrance angle range of α = 0-45°, without particular detriment to statistics. All nuclei with a charge of $Z \geq 18$, which were demonstrated in this range of entrance angles, had energy of 100 to 450 MeV/nucleon. The energy range of demonstrated nuclei broadened and shifted to the right (within the indicated limits) with increase in nucleus charge.

Figure 2 illustrates the differential energy spectrum of iron group nuclei at the location of the detector unit. It was used to plot energy spectrum of the same nuclei falling on the satellite on the assumption that, within the limits of a solid angle with opening α = 45°, the shielding layer can be considered flat, and one can disregard fragmentation of nuclei. The bottom limit of the spectra is attributable to the threshold energy for recording iron group nuclei and the top to the fact that higher energy particle tracks are formed beyond the isolated detector layer. The obtained spectra indicate that, within this range, there is minimal dependence on energy.

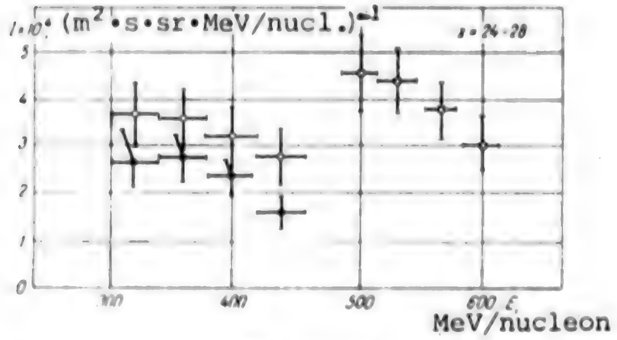

Figure 2.
Differential energy spectra of iron group nuclei. Black circles--instrument spectrum, white--spectrum falling on package; boxes--spectrum falling on satellite

Figure 3 illustrates the charge spectrum of nuclei at the site of the package with energy of 100-450 MeV/nucleon. In scaling [standardizing] the spectrum to time, we took into consideration the following three factors: overall detector exposure time during 19.5-day orbit; shielding of detectors by the earth due to uniform rotation of the satellite about its axis (factor 0.5); the fact that particles with energy of up to 450 MeV/nucleon are transmitted through the unperturbed geomagnetic field only in the orbital phases passing above 50-52° north or south latitude (factor 0.2).

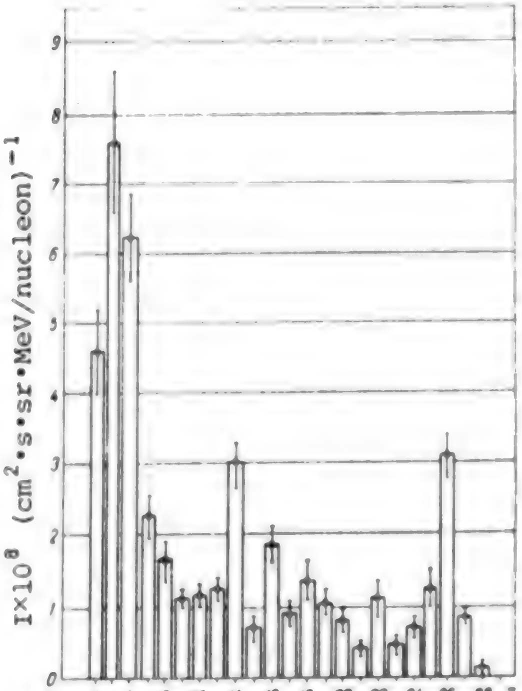

Figure 3.
Charge spectrum

Direct quantitative comparison of our results to those of other authors was impossible, since there are no data in the literature concerning results of analogous measures in orbits of similar parameters. However, the last mentioned factor gives validity to comparison of our data to those obtained from readings taken in the top layers of the atmosphere at latitudes above 50°. A comparison of the results of studies conducted in balloons at an altitude with residual atmosphere of 20-40 kg·m^{-2} in the northern part of the United States and Canada to those we obtained is submitted in Table 1. All of the data were scaled to iron content. The margin of error is 0.05-0.2, and within this range it can be considered that there is rather good agreement of the submitted results. The discrepancy of some data listed in Table 1 is apparently due to differences in exposure periods and conditions under which readings were made.

Table 1. Relative element content

Energy range, MeV/nucleon	Cited work	Nucleus charge								
		20	21	22	23	24	25	26	27	28
200—400	[4]	0,37	0,23	0,51	0,16	0,66	0,61	1	—	—
150—400	[5]	0,41	0,21	0,43	0,12	0,42	0,34	1	—	—
350	[6]	—	—	—	—	0,42	0,60	1	0,25	0,18
100	[7]	0,17	0,18	0,24	0,17	0,38	0,55	1	0,25	0,09
100—150	Our studies	0,28	0,13	0,36	0,15	0,23	0,41	1	0,28	0,03

Table 2. Relative iron isotope content

Residual atmosphere $kg \cdot m^{-2}$	Cited work	Isotope group		
		(52+53)+54	(55)+56+57	58+(59+60)
1,8	[8]	0,38±0,04	0,48±0,04	0,15±0,03
2,0	[9]	0,38±0,08	0,60±0,12	0,10±0,05
3,0	[10]	0,28±0,07	0,43±0,09	0,30±0,07
Cosmos-936 satellite (experiment)	Our data	0,30±0.08	0,49±0,10	0,21±0,05
Theoretical prediction	[11]	0,08	0,92	0,003

We tried to determine in iron nuclei the relative levels of different groups of isotopes.

Table 2 lists the obtained data, as well as results of analogous readings in the upper layers of the atmosphere, which were taken by other authors in recent years. On the whole, all of the experimental data coincide within the margin of error; however, they differ appreciably from theoretically estimated values [11].

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CONDITION OF RAT'S CONNECTIVE TISSUE DURING LONG-TERM HYPOKINESIA AND IN RECOVERY PERIOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 4 Jul 81) pp 73-76

[Article by P. P. Potapov]

[English abstract from source] Changes in the content of collagen (with respect to hydroxyproline), total aminopolysaccharides (with respect to hexosamines), and acid glycosaminoglycans (with respect to hexuronic acids) in the skin and tendons of 102 white rats (including 46 controls) were determined on the 15, 30 and 90th hypokinetic days and on the 15, 30 and 90th days of posthypokinesia recovery. The hydroxyproline content in the skin and tendons did not change. The content of hexosamines and hexuronic acid decreased in tendons on hypokinetic days 15 and 90 and in the skin on day 15. The content of hexosamines in the skin increased on day 90. The content of hexosamines and hexuronic acids in the skin and tendons increased on recovery day 15 and remained unaltered on day 90.

[Text] Prolonged decline of motor activity accelerates processes of natural aging [1, 2]. Decrease in levels of main substance of connective tissue (glycoproteins, glycosaminoglycans) and change in quantitative proportions of these constituents and collagen [3-5] are among the constant disturbances associated with aging. Studies of connective tissue of skeletal muscles and the myocardium under hypokinetic conditions revealed an increase in hydroxyproline/hexuronic acid ratio that is typical of aging [6]. However, it should be borne in mind that the skeletal muscles and myocardium are relatively poor in connective tissue elements. Still unanswered is the question of whether the demonstrated changes are common to all connective tissue of an organism or whether they are manifested only in organs whose main function is related to performance of mechanical work. Our objective here was to study the effects of hypokinesia on composition of skin and tendons, age-related changes in which have been studied well [5].

Methods

This study was conducted on 102 male albino rats (46 of which were controls) weighing 180-210 g. To restrict their movements, the rats were placed in tight individual cages made of plexiglas. The control group of animals was kept in the usual vivarium cages. The rats were decapitated on the 15th, 30th and 90th days of hypokinesia and 15th, 30th and 90th days of the recovery period. Skin taken from the back (from a region that was not in contact with the walls of the small cage while the animal was in it) was shaved and subcutaneous fatty tissue removed. When examining Achilles' tendon, we combined material taken from two animals. After removing fatty tissue and dehydration, we assayed the following in hydrolysates of dry acetone powder recovered from the tissues: hydroxyproline [7], hexosamines [8] and hexuronic acids [9]. Determination of these levels enables us to assess the amount of collagen, total aminopolysaccharides and glycosaminoglycans in tissues.

Results and Discussion

Tables 1 and 2 list the obtained data. Restriction of movement did not elicit an appreciable change in hydroxyproline content of tendons and skin. Hexosamines and hexuronic acids decreased in both tissues on the 15th experimental day. Evidently, a decrease in heteropolysaccharides of connective tissue is typical of the early stages of hypokinesia. Previously, such changes were demonstrated in connective tissue elements of skeletal muscles [6]. In our opinion, increased production of glucocorticoids [10], which depress synthesis of glycosaminoglycans [11], which is observed during the acute period of adaptation to hypokinesia, is the cause of these disturbances.

There was normalization of tissular hexosamine and hexuronic acid content on the 30th day of hypokinesia. On the 90th day, we found changes in different directions in these parameters for the skin and tendons. In the tendon, which had a lower functional load under hypokinetic conditions, hexosamine and hexuronic acid levels were diminished, which led to drastic increase of hydroxyproline/hexosamine and hydroxyproline/hexuronic acid ratios (see Table 2). Thus, we observed changes inherent in aging connective tissue in the tendon during long-term hypokinesia. During this period, there was some elevation of aminopolysaccharide levels.

There was drastic increase in glycosaminoglycan content of tendons and skin on the 15th day of the recovery period, as compared to both the control and 90th day of hypokinesia. Changes in a similar direction at comparable times had also been demonstrated previously in skeletal muscles and the myocardium [6]. It can be assumed that they were related, in part, to impairment of fluid-electrolyte balance. Under hypokinetic conditions, increased diuresis, moderate dehydration of tissues and decreased amount of extracellular fluid were demonstrated in rats and rabbits [12-14]. After termination of hypokinesia, there was drastic decline of diuresis [13], which is perhaps indicative of fluid retention. Tissular glycosaminoglycans play a substantial role in binding and transporting fluid and inorganic ions; however, the capacity to bind fluid depends appreciably on the length of their molecules [15]. We know from the literature [16] that, at the early stages of the recovery period, there is less production of glucocorticoids, which depress synthesis of glycosaminoglycans and increase polymerization thereof [11]. For this reason, fluid retention (rehydration) in tissues at the early stages of the recovery period requires more than normal heteropolysaccharides in connective tissue. Thus, in this case, the rise in level thereof is adaptive in nature.

Table 1. Hydroxyproline, hexosamine and hexuronic acid levels in rat skin during hypokinesia and recovery period (in μM/g dry defatted tissue)

Parameter	Rat group	Hypokinesia, day			Recovery period, day		
		15	30	90	15	30	90
Hydroxyproline (HO)	Control	798±19 (8)	798±19 (8)	808±10 (8)	808±10 (8)	8[illegible]1±22 ([illegible])	851±20 (8)
	Experiment	825±17 (8)	800±16 (8)	770±20 (8)	717±41 (6)	833±23 ([illegible])	877±19 (8)
Hexosamines (HA)	Control	34,7±1,0 (8)	34,7±1,0 (8)	36,0±1,2 (8)	36,0±1,2 (8)	30,0±0,7 ([illegible])	29.9±0.8 (8)
	Experiment	31,2±1,1 (8)•	35,2±1,4 (8)	40,3±1,7 (8)•	46,4±2,3 (6)•	32,3±0,6 (6)•	30.6±0.9 (8)
HO/HA	Control	22,8±0,8 (8)	22,8±0,8 (8)	22,4±1,3 (8)	22,4±1,3 (8)	28.7±0,9 (6)	28,4±1.0 (8)
	Experiment	26,4±1,0 (8)•	22,9±1,3 (8)	19,1±1,6 (8)	15,5±2,4 (6)•	25,8±0,9 ([illegible])•	28,6±1,3 (8)
Hexuronic acids (HUA)	Control	21,6±0,4 (8)	21,6±0,4 (8)	21,2±0,4 (8)	21,2±0,4 (8)	20,9±0,5 (6)	20,0±0.3 (8)
	Experiment	19,5±0,7 (8)•	21,5±0,4 (8)	22,5±0,5 (8)	28,3±1,1 (6)•	23,2±0,8 (6)•	20,5±0.6 (8)
HO/HUA	Control	35,9±1,2 (8)	35,9±1,2 (8)	38,1±0,8 (8)	38,1±0,8 (8)	41,0±1,2 (6)	42,6±0,8 (8)
	Experiment	41,3±1,4 (8)•	36,4±1,0 (8)	34,2±1,0 (8)•	25,6±2,0 (6)•	35,2±1,7 (6)•	41,8±1,1 (8)

Note: Here and in Table 2, number of animals in group is given in parentheses. Asterisks refer to statistically reliable differences from the control.

Table 2. Hydroxyproline, hexosamine and hexuronic acid levels in rat tendons during hypokinesia and recovery period (in μM/g dry defatted tissue)

Parameter	Rat group	Hypokinesia, day			Recovery period, day		
		15	30	90	15	30	90
Hydroxyproline (HO)	Control	986±11 (5)	985±11 (5)	979±27 (6)	979±27 (6)	974±30 (6)	968±25 (6)
	Experiment	992±33 (5)	962±22 (5)	998±34 (5)	962±42 (4)	982±45 (4)	978±39 (5)
Hexosamines (HA)	Control	27,8±0,5 (5)	27,8±0,5 (5)	29,0±1,2 (6)	29,0±1,2 (6)	28.5±0,9 (6)	27,9±1,0 (6)
	Experiment	25,8±0,5 (5)•	26,9±1,0 (5)	26,5±1,0 (5)	30,4±1,1 (4)	28,7±1,2 (4)	26,1±1,1 (5)
HO/HA	Control	35,4±0,8 (5)	35,4±0,8 (5)	33,8±1,3 (6)	33.8±1,3 (6)	34,2±1,1 (6)	34.7±1,2 (6)
	Experiment	38,4±0,9 (5)•	35,7±1,2 (5)	37,7±1,1 (5)•	31,6±1,3 (4)	34,2±1,4 (4)	37,5±1,4 (5)
Hexuronic acids (HUA)	Control	19,5±0,4 (5)	19,5±0,4 (5)	19,4±0,5 (6)	19,4±0,5 (6)	19,5±0,7 (6)	19,3±0,5 ([illegible])
	Experiment	17,5±0,5 (5)•	18,9±0,6 (5)	17,1±0,8 (5)•	22,0±0,9 (4)•	19,4±0,8 (4)	18,2±0,6 (5)
HO/HUA	Control	50,5±1,2 (5)	50,5±1,2 (5)	50,5±1,0 (6)	50,5±1,0 (6)	49,9±1,7 (6)	50,2±1,2 (6)
	Experiment	56,7±1,8 (5)•	50,9±1,6 (5)	58,4±1,8 (5)•	43,7±1,9 (4)•	50,6±2,1 (4)	53,7±1,4 (5)

There was normalization of aminopolysaccharide content in tendons on the 30th day after returning the animals to the usual living conditions, whereas it remained high in the skin, although there was a tendency toward decline, as compared to the 15th day of the recovery period. We failed to demonstrate reliable changes in the parameters studied on the 90th day of the readaptation period.

The results submitted here, as well as previously obtained data [6], warrant the conclusion that there may be disturbances, which are typical of aging, in functionally inactive tissues (skeletal muscle, myocardium, tendon) during prolonged restriction of movements. However, these changes are reversible; 90 days after hypokinesia, the animals failed to present appreciable changes in normal proportions of the main substance and fibrous elements of connective tissue.

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OSTEOPOROSIS IN UNSUPPORTED EXTREMITIES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 6 Apr 81) pp 76-82

[Article by A. I. Volozhin, G. P. Stupakov, A. N. Polyakov, S. M. Remizov, M. N. Pavlova and I. Ye. Didenko]

[English abstract from source] In dogs, the lower part of the right extremities was amputated, thus generating a support-free state of the femur. On day 90 after the amputation bone resorption reached a high level and by the end of the year declined. The mature bone microstructures showed a higher degree of mineralization, whereas the young bone microstructures which were in predominance in the support-free femur displayed a lower degree of mineralization. In bone, the content of Ca decreased, that of K increased, while the content of Na and P remained unchanged. The development of osteoporosis in the support-free femur did not involve only quantitative variations in the mineral components.

[Text] Dystrophic changes in bone tissue, which were classified as osteoporosis, have been demonstrated under the influence of spaceflight factors and model experiments where the bearing function of bones was eliminated [1-3]. Development thereof is attributable to activation of bone tissue resorption with concurrent loss of minerals and organic substances. On this basis, it can be assumed that the reduction in bone mass in the presence of osteoporosis occurs without appreciable changes in minerals [4, 5]. However, there are no data to prove this thesis. We are concerned here with settling this matter.

Methods

Experiments were conducted on 8 dogs 1.5-4 years of age. The lower third of the right leg was amputated under thiopental anesthesia and aseptic conditions. The muscles were sutured with catgut and silk sutures were applied to the skin. The wound healed by first intention. The dogs were sacrificed on the 90th and 345th postoperative days (equal number of dogs at each time) with ether and chloroform vapor, both femurs were cleared of soft tissue and stored in 1% neutral formalin.

The right (unsupported) bone was considered experimental and the left, the control. The bones were x-rayed in anteroposterior and lateral projections, then, using an MBS-2 microscope with a metric scale, we determined on the x-rays the outside width, thickness of cortical layer and width of medullary cavity strictly in the center of the diaphysis (margin of error ±0.05 mm). For further examination, we cut out circular fragments in the middle third of the diaphysis using a metal cutter. Histological specimens were prepared from bone fragments decalcified in 7% nitric acid. Sections 8-10 μm in thickness were stained with hematoxylin and eosin, picrofuchsin and according to Schmorl. We measured the area of vascular canal lumen on histological preparations by means of a morphological grid [6] attached to the microscope ocular (7×), with 90× objective. The measured vascular canals were ranked according to cross-section: up to 51, 105, 154, 205, 256, 307, 410 and up to 614 μm^2. The results were expressed as percentage of all canals counted in the preparations.

Table 1. Changes in cross sections of femoral diaphyses of dogs with limbs in unsupported position (mm)

Group	2I	D	d	i
a-p projection 90 days				
Control	4,15±0,11	9,60±0,20	5,45±0,14	0,42±0,008
Experiment % of control	3,77±0,27 90,8	9,60±0,21 100	5,82±0,15 106,8	0,39±0,019 92,8
345 days				
Control	3,97±0,15	10,92±0,27	6,95±0,42	0,37±0,023
Experiment % of control	2,85±0,18 71,8	10,72±0,33 98,2	7,87±0,41 113,2	0,27±0,021 73,0
lateral projection 90 days				
Control	3,86±0,01	8,92±0,35	5,06±0,32	0,43±0,015
Experiment % of control	3,61±0,21 93,5	8,92±0,37 100	5,31±0,35 104,9	0,41±0,023 95,3
345 days				
Control	4,12±0,13	11,30±0,55	7,17±0,45	0,37±0,010
Experiment % of control	2,77±0,19 67,2	11,15±0,62 98,7	8,37±0,67 116,7	0,25±0,022 67,6

Key: 2I) thickness of cortical layer
D) outside width of bone
d) width of marrow cavity
i) 2I/D ratio

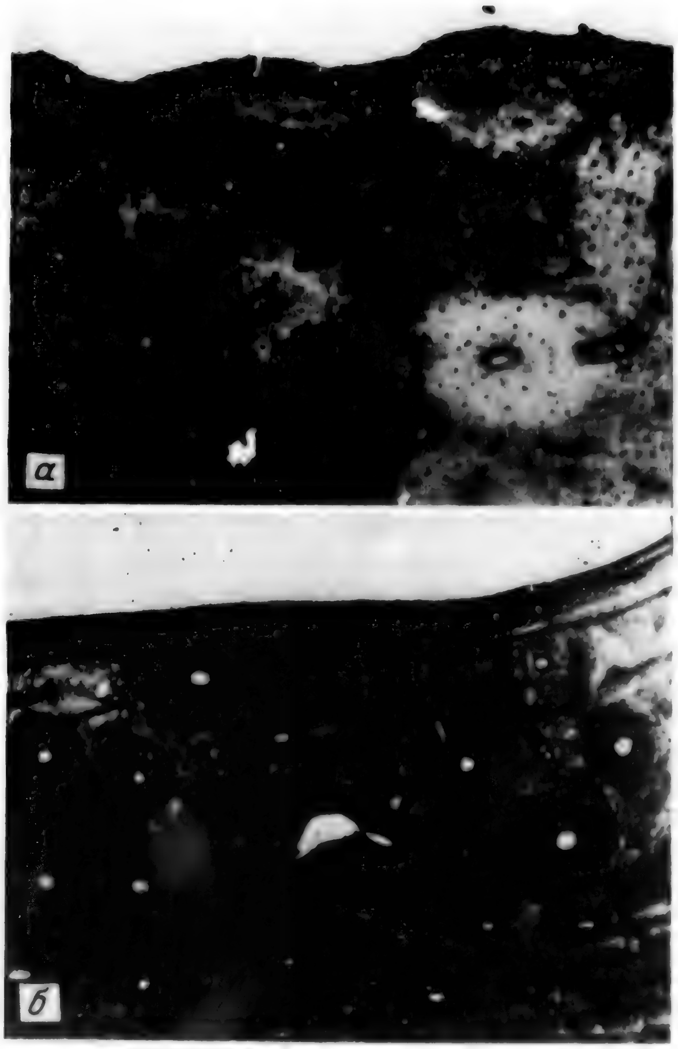

Figure 1. Segment of section of dog's femoral diaphysis on the side of the endosteal surface 345 days after amputation
Here and in Figure 2:

a) unsupported extremity (experiment) b) bearing limb (control)

There are no general lamina on the side of the marrow cavity. No areas of resorption deep in the bone are seen. Hematoxylin and eosin stain. Magnification 90×

Table 2. Changes in density, mineralization and ash content of compact and spongy substances of dog's femurs with unsupported extremity

Hypo-dynamia, days	Group	Diaphyseal compact bone			Distal epiphyseal spongy bone		
		density, g/cm^3	mineralization g/cm^3	ash content, %	density, g/cm^3	mineralization g/cm^3	ash content, %
90	Control	1.853±0.044	1.166±0.030	63.15±0.23	0.439±0.012	0.262±0.008	59.68±0.54
	Experiment % of control	1.740±0.036 93.9**	1.098±0.025 91.2**	62.90±0.52 99.6	0.298±0.021 67.9**	0.176±0.011 67.2**	59.30±0.80 99.4
345	Control	1.893±0.033	1.226±0.021	64.63±0.34	0.41[illegible]±0.021	0.245±0.013	59.28±0.79
	Experiment % of control	1.875±0.053 99.8	1.190±0.036 99.1	63.48±0.23 98.2	0.263±0.02[illegible] 63.5**	0.151±0.015 61.[illegible]**	57.10±1.38 96.3

For quantitative evaluation of porosity of cortical bone and distal epiphysis, we determined the density (in g/cm^3) and volume of minerals (mineralization, g/cm^3) using a previously described method [7]. Mineralization of organic bone was determined from ash content (ratio of mineral mass to mass of dry, defatted bone fragment). We submitted polished sections of the dogs' diaphyses to microroentgenographic analysis using our modification of the conventional method [8].

We determined the microhardness of bone tissue in polished sections, which were defatted and desiccated at a temperature of 20-22°C, imbedded in "protacryl" plastic [9]. We made 20 indentations on each sample with the diamond pyramid-shaped indenter of a PMT-3 instrument at a pressure of 100 Gs [gram-centimeter?].

Determination was made of mineral elements on an atomic absorptiometer, phosphorus was assayed on a spectrophotometer using sodium molybdenate. Potassium and sodium were assayed on a flame photometer [10]. The results were submitted to processing by parametric and nonparametric statistical methods.

Results and Discussion

Absence of support elicited a decrease in bone mass, as compared to the control (bearing limb), as indicated by thinning of the cortical layer on the side of the marrow cavity, without change in outside width of the diaphysis. These changes in the unsupported bone were particularly evident in the 345-day experiment (Table 1). There was an increase in width of the medullary canal corresponding approximately to the reduction in thickness of the cortical layer, due to intensified resorption of diaphyseal bone tissue, mainly on the side of the endosteum. Thus, on the 90th experimental day, diaphysis preparations showed an increase in lacunar resorption of bone tissue with involvement of polynuclear osteoclasts. The considerable area of resorption zones deep in the cortical layer explains the decrease in density of cortical bone on the 90th experimental day (Table 2). On the 345th day of the experiment, the thickness of the cortical layer of the diaphysis of the unsupported femur was thinned down more than at the previous examination. However, the density of the unsupported limb corresponded to the control, as confirmed by histological examination, which demonstrated absence of resorption zones deep in the bone (Figure 1, a and b).

Impairment of reorganization of bone tissue due to absence of support can be seen from the results of morphological examination of histological sections. Asymmetrical distribution of canals according to area was established in the bone of the control extremity. About 77% of all vascular canals had an area of less than 154 μm^2, and there were only about 23% of the canals that had larger areas, the share of canals with an area of 614 μm^2 or more constituting only 4.4%, which is indicative of rather slow reorganization of osseous tissue on the supported side in adult animals.

After 90 days of unsupported position of the limb, we demonstrated an 18% increase in number of the smallest (less than 51 μm^2) vascular canals in the bone. As compared to the control, there was an 8% increase in number of largest canals.

The relative increase in number of small canals at this stage of the experiment could be attributable to intensification of resorption in the subendosteal region, as a result of which mainly the osteon systems with large vascular canals localized near the medullary cavity "disappear." On the 345th day, the distribution of the vascular canals changed: considerable decrease in relative number of small canals due to increase in number of medium and large ones, which is indicative of intensified resorption of bone tissue.

Unlike the morphological findings, the results of microroentgenographic examination of osseous tissue enabled us to demonstrate quantitative changes in microstructural minerals. Three months after amputation, visual examination of the entire area of the polished section of diaphysis from the unsupported limb on the microroentgenogram enabled us to detect signs of an osteoporotic process. At the same examination time, none of the microroentgenograms showed de novo osteons with low mineral density, which confirms the drastic depression of osteogenesis.

On sections of bone from the unsupported limb referable to the 345-day experiment, there are quite a few osteons with diminished mineralization, as compared to interstitial lamellae (Figure 2a). These osteons were encountered in groups, in some parts of the transverse diaphyseal section, particularly on the side of endosteum. In osseous tissue from the control extremity, the osteons essentially retained a high degree of mineralization (Figure 2b). For this reason, the microroentgenographic studies were made in two methodological modifications.

In the first place, we determined separately the mean mineralization of highly and poorly mineralized microstructures: interstitial lamellae and osteons.

In the second place, we determined the mean mineralization of areas of active regeneration of the section. This variant of analysis was used only in the 345-day experiment, since most of the osteons were fully mineralized after the 90th experimental day. Thus we assessed the direction of bone reorganization and dynamics of mineralization of microstructures determined by it over a specific segment of the diaphysis.

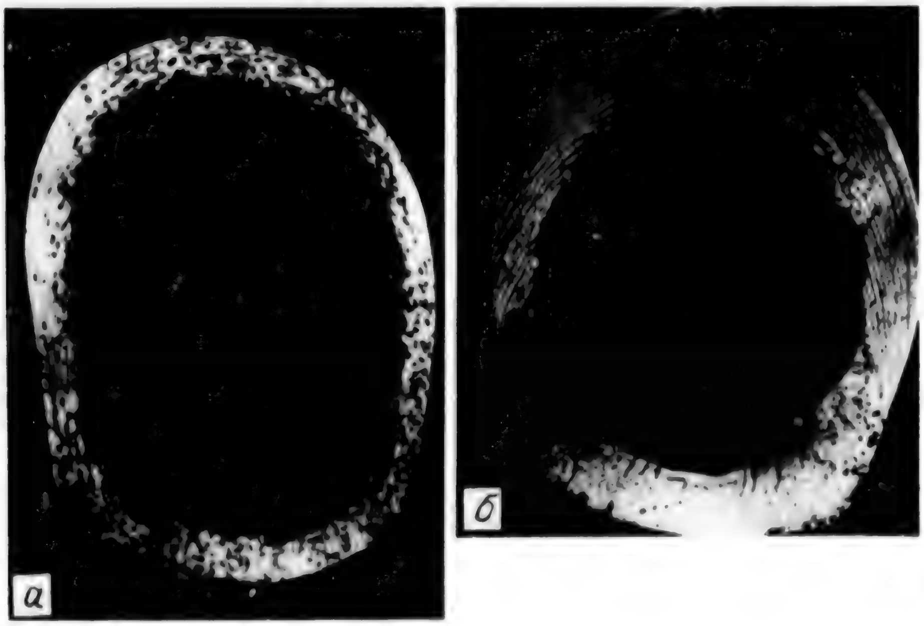

Figure 2. Microroentgenographs of sections of dog's femoral diaphyses 345 days after surgery (magnification 7×)

Average mineralization of mature osteons and interstitial lamellae making up most of the bone in the unsupported limb in the 90-day experiment was insignificantly greater (by 0.02 g/cm^3) than in the control. This difference increased to 0.06 g/cm^3 in the 345-day experiment. Evidently, this tendency toward increase in minerals of microstructures in the unsupported bone can be attributed to a passive (on the order of deposition of salts in oversaturated solutions) mechanism, which is present when there are microcirculatory changes in some parts of a bone.

In the part of the section where mineralization of osteons differed from that of interstitial lamellae, average mineralization at both stages of the experiment was virtually the same in the experimental and control limbs.

In view of heterogeneity of the microroentgenographic image of the bone in the 345-day experiment, where there were areas of reorganization of osseous tissues with many young osteons with low mineral density, it was interesting to make an integral evaluation of mineralization of these areas without morphological differentiation, i.e., without separation into osteons and interstitial lamellae. The obtained data revealed distinctions in bone reorganization.

Table 3. Changes in mineral composition of spongy and compact substances of dog femur with unsupported extremity

Bone part	Hypodynamia, days	Group	Element content/100 g ash			
			Ca	P	Na	K
Diaphysis	90	Control	41,48±1,36	14,15±0,24	460,0±28,8	48.7±1,50
		Experiment % of control	39,70±0,88 95,7	14,58±0,35 103,0	486,0±15,3 105,6	74,50±5,96 152,9**
	345	Control	42,53±0,44	15,43±0,96	494,5±26,0	55,85±9.17
		Experiment % of control	41,15±0,34 96,7*	15,38±0,44 99,7	453,1±22,8 91,6	77,38±13,17 138,5
Epiphysis	90	Control	41,27±0,85	14,93±0,61	595,0±31,1	34,60±3,49
		Experiment % of control	39,37±1,08 95,4*	14,80±0,36 99,1	555,8±9,6 93,4	52,98±2,53 153,1**
	345	Control	40,98±0.76	14,43±0,30	437,1±37,1	55,20±14,35
		Experiment % of control	39,80±1,29 97,1	15,20±0,65 105,3	488,1±17,8 111,7	50,17±4,20 90,9

*P<0.05 **P<0.01

These results indicate that the mean mineralization of the segment of the section was lower on the "unsupported side" than the control. According to A. V. Rusakov [11], the process of resorption of bone tissue is always associated with de novo formation thereof. However, in the case of loss of function of an osseous organ, the rate of maturation of bone tissue can slow down significantly.

Analysis of the data revealed that there is a decline in average microhardness in bone tissue of the femoral diaphysis of the unsupported limb, as compared to the control on the 90th and 345th days. These changes are due to the fact that we encounter many microsegments with diminished microhardness on the bone section from the unsupported extremity, as compared to other segments. In reflected light at a magnification of 480×, these segments appear as clear points, which apparently represent osseous microstructures with low mineralization.

The decrease in microhardness was also demonstrated in the nonosteonic spongy bone tissue of the epiphysis of the amputated extremity, as compared to the control.

The disturbances referable to organization and mineralization of bone tissue as a result of being in an unsupported position for a long time were associated with consistent changes in mineral composition (Table 3). At both observation times, there was a decrease in Ca content of both compact and spongy bone tissue. Another distinction of mineral composition of the unsupported limb was a higher K content than in the control. P content did not change, and for this reason there was a change in Ca and P ratio. This is attributable to the fact that excessive mineralization ("salination") of mature structures was due not only to crystals but amorphous calcium phosphate, which has a lower Ca and P ratio than hydroxyapatite [12].

These changes may also be related to structural change in hydroxyapatite or increase in proteins with high P content.

Thus, use of a combined methodological approach enabled us to demonstrate several new patterns in the mechanism of development of osteoporosis during prolonged absence of supporting function in an extremity. The high resorption activity of bone tissue, which was observed during the first few months, gradually diminished and, at 1 year, perhaps tended toward reaching a level, to maintain which neither locomotor acts nor a force load are required.

Since femoral hypodynamia was produced by amputating the leg, the rate of resorptive processes under such conditions is apparently at a maximum.

The developing osteoporosis is characterized not only by quantitative changes in osseous tissue, which consist of reduction of bone mass, but qualitative changes. This is manifested by a change in proportion of osteons differing in degree of mineralization. The higher mineralization of mature osteons could be attributed to the fact that these microstructures existed before the unsupported position was created, they persisted at the end of the experiment and, perhaps, were subject to additional mineralization.

Other distinctive features of bone tissue of the unsupported limb are an increase in number of microstructures with low mineralization and decrease in their mean density in some segments of the bone in the 345-day experiment. Perhaps these microstructures, which developed during the period of unsupported position of the extremity, have a slower capacity for mineralization. The proportion of different osteons in different segments of sections of this bone changes in the direction of immature microstructures, which is manifested by a decrease in mean mineralization of bone tissue and microhardness.

To sum up our findings, we can expound the hypothesis that drastic decrease of afferentation from the bone, as a result of which there is no trophic reflex [13], as well as a piezo effect, which depends on periodic loads on the bone, play the leading role in the mechanism of change in minerals and reorganization of bone tissue in an unsupported extremity.

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METHODS

UDC: 629.78:616.281/.282-089.87:616.832.74]-092.9

PREPARATION OF LABYRINTHECTOMIED ANIMALS FOR FLIGHT ABOARD COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 10 Apr 81) pp 83-86

[Article by A. R. Kotovskaya, Ye. A. Savina, A. V. Mokrousova, Ye. I. Alekseyev, A. S. Markin, V. F. Anichin, A. A. Shipov and G. S. Ayzikov]

[Text] The program of experiments aboard the Cosmos-936 biosatellite provided for having labyrinthectomied animals (LA) aboard the biosatellite [1]. It was assumed that examination of LA after the space flight would make it possible to assess the role of the vestibular system in the complex reactions to long-term weightlessness. Such studies had been conducted only in experiments involving brief exposure to weightlessness, and they revealed that LA endure weightlessness much more calmly and easily.

Preparation of LA for the space flight included solving the following problems: refine the technique and perform effective labyrinthectomy on animals, monitor their condition in the postoperative period. This article is concerned with analysis of the results of these studies.

Methods

We used male albino Wistar-SPF laboratory rats in the main experiments (flight and control) [1]. The techniques for labyrinthectomy and postoperative examination were refined on mongrel, Wistar and Wistar-SPF rats.

Labyrinthectomy: It was based on the principle of local electrocoagulation of the sensory epithelium of the membranous labyrinth [2]. The specific distinctions of such operations on albino rats were described previously [3]. In the course of refining the technique, the labyrinths were inactivated on one or both sides. In the latter case, the operations were performed bilaterally at the same time, or else the healthy labyrinth was coagulated several days after unilateral labyrinthectomy. The rats in the flight and control groups underwent simultaneous inactivation of the labyrinths 14-15 days before the spaceflight or start of synchronous experiment.

Clinical and physiological studies: These studies included general and otological examination, clinical vestibular and vestibulomotor tests, analysis of postural, motor and behavioral reactions. Special equipment was used to test elevator and rolling-over reflexes, as well as equilibrium [4-6]. Nystagmography was used to demonstrate spontaneous and postrotation nystagmus. In developing the labyrinthectomy technique, animals with unilateral and bilateral labyrinthectomy were followed up for 1-2 months. The animals of the flight and control groups were examined during the postoperative and preflight periods daily, for a period of 14-15 days.

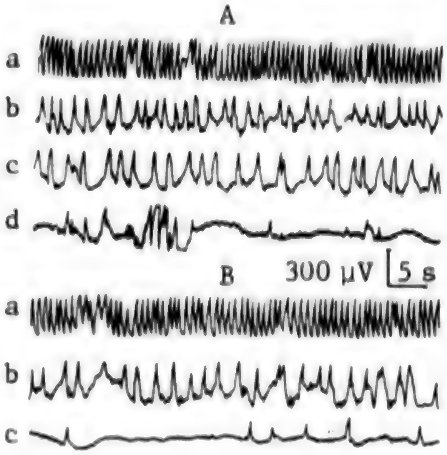

Figure 1.
Nystagmograms of rat at different times after unilateral (A) and bilateral (B) labyrinthectomy
a-d) 2 h, 1, 2 and 3 days, respectively, after surgery

Morphohistological examination: The temporal bones were excised 1.5-2 min after decapitating the animals; they were immersed in heated Vitmak fixing mixture, then decalcified, washed in tap water, dehydrated in alcohol and saturated with celloidin [7]. Serial sections (10 μm) on the cochlea-vestibule level were oriented in the sagittal plane: they traverse the cochlea in a longitudinal direction and the sacculi transversely. The preparations were stained with hematoxylin-eosin.

Results and Discussion

Clinical and physiological data: Clinical signs of labyrinthectomy were the same in all animals; however, their duration and severity presented some individual distinctions. After unilateral

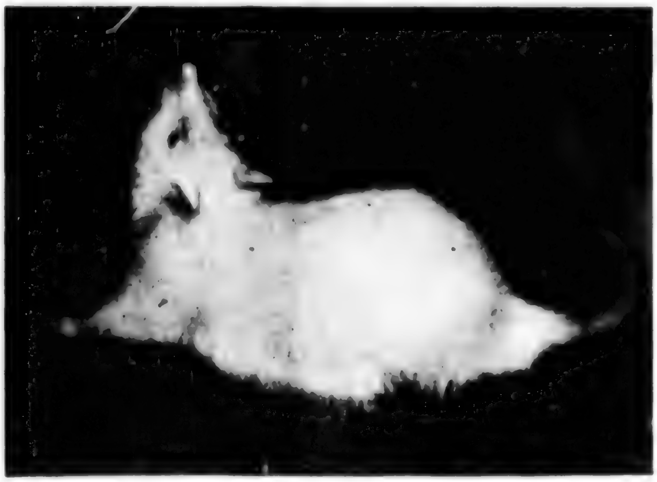

Figure 2. Appearance and typical position of rat after bilateral labyrinthectomy

labyrinthectomy, we observed tonic deviation of the eyes, spontaneous nystagmus, inclination of the head and body. Tonic deviation of the eyes was demonstrable in most animals immediately after coming out of the anesthesia. In rare cases it occurred already when current was used during electrocoagulation. Spontaneous nystagmus also appeared after waking from anesthesia, persisting for 2-3 days (Figure 1A). On the 1st day after inactivation of the labyrinth, nystagmus was present in all animals. Its mean frequency constituted 138.9±2.4/min 2 h after surgery and 50.4±1.1/min by the end of the first day. Nystagmus persisted, with a mean frequency of 27.3±0.7/min, in 84.2% of the animals on the second day. In some animals, this sign was also observed on the 3d postoperative day, but it was mild.

Inclination of the head to the side of the inactivated labyrinth, as well as the above-mentioned symptoms, appeared after coming out of the anesthesia. It was usually associated with extension of the contralateral extremities and inclination of the trunk. In some cases, the animals lay on their side or rolled over on the side of the inactivated labyrinth for 1-3 h after the operation. All animals presented circular (in a ring) movements in the direction of the inactivated labyrinth for 3-6 h, sometimes 1-2 days after the operation. Analogously, rats suspended by the tail with the head down, made rotating movements about the longitudinal axis of their body in the direction of the inactivated labyrinth. This symptom appeared 1 day after the operation (less often after 3-4 h) and was demonstrable throughout the observation period (1-2 months).

Electrocoagulation of the second labyrinth was performed 5-7 days after the first operation. Again there was tonic deviation of the eyes, inclination of the head in the direction of the second inactivated labyrinth for 1-2 days, circular movements for 3-4 h after coming out of the anesthesia. In addition, we observed restless behavior, nystagmoid twitching of the head, backward movements (when placed on a laboratory table, the rats started moving backward without any apparent cause). After awaking, all of the animals developed spontaneous nystagmus in the direction of the previously inactivated labyrinth, which lasted for about 2 days (Figure 1B). It persisted for 1 day in 89.5% of the cases and for 2 days in 57.9%. Frequency of nystagmus constituted 113.1±2.5/min 2 h after the operation, 41.7±1.3 on the 1st day after surgery and 12.6±0.7/min on the 2d day.

After simultaneous total inactivation of both labyrinths, the above-described signs for unilateral labyrinthectomy were not demonstrable. We were able to observe nystagmoid twitching of the head, backward movements for several days (1-3) of the postoperative period, but they gradually regressed and disappeared completely at the end of the 1st week.

By the end of the 2d postoperative week the rats' behavior was characterized by increased motor activity, and their general condition was good. They moved about continuously and haphazardly, stopped abruptly, reversed direction of movement, as if scouring about. Occasionally they moved in a circle, but without dominant direction. Movements were abrupt, angular and often uncoordinated. They threw their head back and presented ataxia (Figure 2). Equilibrium was drastically impaired: they could not stay on a narrow bar

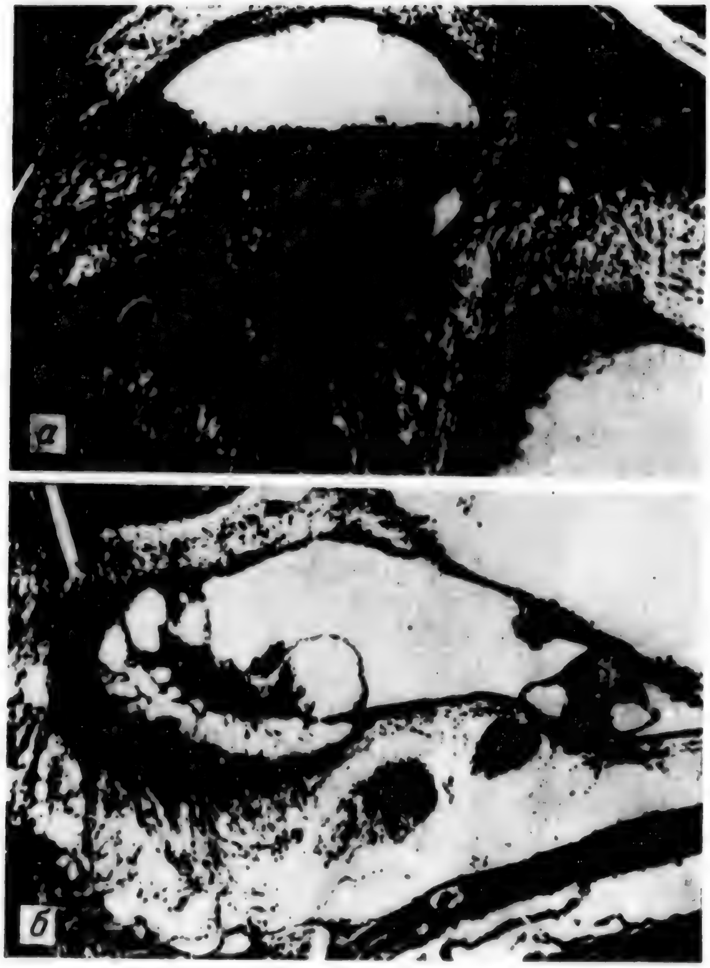

Figure 3. Histological appearance of vestibular analyzer of labyrinthectomied rats. Hematoxylin-eosin stain; objective 6.3×; ocular 6.3×

a) saccular segment: massive proliferation of granulation tissue in the place of the membranous labyrinth
b) utricular segment: degenerative changes in the macula and ampullar crista

and fell down. Loss of equilibrium was also observed when they walked and made rapid turns. There was no elevator reflex. The reaction of rolling over from supine position in free fall was absent when they could not see (small hood placed over the head to cover the eyes), and when they could see we sometimes merely observed an attempt to roll over, but they did not land on their legs.

As can be seen from the submitted data, the rats' reactions to inactivation of the labyrinths were similar to the analogous reactions of other animals, for example cats or guinea pigs [8, 9]. This is indicated by the time and distinctions of compensation of the vestibular defect in the case of unilateral labyrinthectomy, appearance of Bekhterev's phenomenon in the case of separate inactivation of the labyrinths and, finally, persistent and marked somatoneurological signs after simultaneouls total labyrinthectomy. In the latter case, we should mention the good appearance of the animals, normal weight gain, absence of any vegetosomatic sequelae of the surgery proper--postoperative inflammation or infected wound process. The rats were essentially in good health prior to the spaceflgiht. The only exception was referable to the specific symptoms characterizing bilateral loss of labyrinths.

Proceeding from the clinical and physiological findings, it can be stated that the labyrinthectomy method we chose--electrocoagulation--is quite reliable and effective. For definitive evaluation of the surgical results, we used the following signs of total inactivation of the vestibular system, which we consider important: absence of symptom of rotation and "ready to jump" reflex when the rats are upside down (usually the experimenter held the animal by the tail, suspending it), absence of reflexes to motions with variable velocity, as well as compensatory shifting of the eyes in response to slow inclinations and change of position, absence of spontaneous and postrotation nystagmus, inability to hold on to a rocking platform when it is tilted slowly or rapidly [10]. If there was any doubt as to the success of labyrinthectomy, the rats were discarded. The reliability of clinical and physiological evaluation of labyrinthectomy was checked morphologically, which enabled us to determine the degree of observed damage.

Morphological data: We examined 26 labyrinths, 21 of which presented pathological changes in structural organization of the vestibular system. Partial labyrinthectomy was found in 7 cases and total in 14 (in 8 animals there was bilateral involvement and in 6 unilateral). Morphologically, labyrinthectomy was manifested by impairment of anatomical integrity of the vestibule, obliteration of the perilymphatic space of the membranous labyrinth, destruction of receptor elements of the sacculus, utriculus and ampullae of semicircular canals. A very typical finding was the presence of changes in the osseous labyrinth near the base of the cochlea. Depending on their extensiveness, the pathological changes were either localized in the sacculus or extended to other structures of the vestibular system (utriculus, semicircular canals). In the case of partial labyrinthectomy, the morphological changes were demonstrable mainly in the sacculus and consisted of massive proliferation of connective tissue in the perilymphatic space and atrophy of macular receptor epithelium.

The greatest changes were observed in the case of total labyrinthectomy. There was virtually total closure of the membranous labyrinthine cavities in the saccular region, which were filled with dense granulation tissue, with preservation of areas of endolymphatic space (Figure 3a). Massive proliferation of granulation tissue in the saccular membranous labyrinth extended to the perilymphatic space of the utriculus and semicircular canals. In the utricular macula, there was separation of receptor cells from their connective tissue matrix, with destruction of the basilar membrane and receptor epithelium. There were degenerative changes in receptor cells in the ampullar cristae of the semicircular canals and desquamation of transitional epihtelium at the base of the cristal stroma (Figure 3b). After labyrinthectomy, we also demonstrated appreciable changes in structures of the hearing system: extensive sites of damage to the osseous labyrinth, proliferation of granulation tissue in the perilymphatic and endolymphatic ducts, destruction of the cochlea. However, according to morphohistological findings, in all cases the destructive processes did not exceed the limits of the labyrinth.

Thus, electrocoagulation led to significant destruction of labyrinths in both the vestibular and auditory segments. The severity and extensiveness of the changes were related to precision of applying the active electrode to the base of the cochlea, as well as force and duration of electric current passed through the labyrinth during the operation. Clinicophysiological analysis of the effectiveness of inactivating the vestibular system revealed that it was quite successful and entirely verified by morphohistological findings. The preflight status of labyrinthectomied animals was characterized by good general condition and marked somatoneurological signs due to bilateral loss of labyrinths.

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UDC: 629.78:612.111.3

METHODOLOGICAL ASPECTS OF TESTING ERYTHROCYTE BALANCE BY COUNTING INCUBATED RETICULOCYTES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 25 Aug 81) pp 86-88

[Article by A. V. Ilyukhin, T. Ye. Burkovskaya, A. V. Shafirkin and N. V. Klyuchanskaya]

[Text] At the present time it can be considered certain that when man spends a long time in space, as well as under conditions simulating weightlessness, there is impairment of erythropoiesis ultimately leading to decline of erythrocyte mass [1-3]. In view of the realistic possibility of extending spaceflights, the problem of determining the mechanism of development of erythrocyte deficiency is very acute.

One of the mandatory conditions for assessing functional activity, reserve potential and mechanisms of development of various disturbances in the erythron system is to investigate the correlations between cytokinetic parameters of erythrocyte balance.

It is known that quantitative evaluation of erythrocyte balance can only be made by using reliable cytokinetic methods for examining erythropoiesis and dieresis. The widely used techniques involving intravital labeling of erythrocytes with radioactive isotopes are reliable enough, but not indifferent to the body. The method of determination of erythrocyte life span on the basis of rate of maturation of reticulocytes in vitro according to Ye. N. Mosyagina [4-6] is the most convenient for the patient and, consequently, suitable for space research purposes. However, use of this method revealed flaws, which compelled us to search for a way to refine it.

Methods

The technique of Ye. N. Mosyagina is based on the assumption that equiponderant erythrocyte balance, which assures a constant erythrocyte level in blood, is characterized by an equal quantity of erythrocytes entering the blood stream and broken down in an equal period of time. A change in any element of the kinetics (decline or intensification of proliferative activity, faster or slower differentiation of erythrocyte precursors, change in erythrocyte life span, etc.) leads to impairment of equilibrium, which is manifested by a change in erythrocyte content of peripheral blood. The quantity of reticulocytes that mature per unit time is the quantitative gauge of erythropoiesis. The difference in reticulocyte content before and after incubating blood enables us to assess the quantity of erythrocytes entering the blood stream or destroyed in this period of time.

It is known that the curve of decline in reticulocyte content N_r as a function of time during incubation in vitro is nonlinear. The author of the technique considers it to be linear over a limited initial segment, in the belief that the velocity of decline V of absolute number of reticulocytes is constant, and he extends the initial tendency to the next time intervals, on the basis of the following equation:

$$N_r = N_{r_0} - Vt \qquad (1)$$

The author describes a method for determining some of the parameters of erythrokinetics on the basis of initial number of reticulocytes N_{r_0} and number of reticulocytes after incubation for 4 h. Thus, to calculate reticulocyte maturation time T_r, he uses a graphic plot and boundary approximation of the above equation:

$$T_r = \frac{N_{r_0}}{V} \text{ with } t = T_r,\ N_r = 0 \qquad (2)$$

and he determines bone marrow production of erythrocytes scaled to 1 μℓ blood per day on the basis of velocity of reticulocyte reduction, according to the following equation:

$$P = \frac{(N_{r_0} - N_{r_4})N_{er} \cdot 24}{4 \cdot 1000} \qquad (3)$$

where $\frac{N_{r_0} - N_{r_4}}{4} = V$ is mean speed of reticulocyte maturation per hour, N_{er} is quantity of erythrocytes per μℓ blood. Graphic determination of reticulocyte maturation time by the method of Ye. N. Mosyagina is illustrated in Figure 1a.

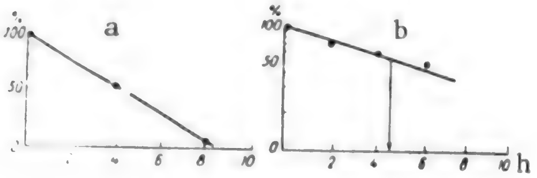

Figure 1.
Absolute (a) and relative (b, %) change in reticulocyte number as a function of time during incubation
T_r = 8.5 h (calculated from a)
$T_{½r}$ = 4.7 h (calculated from b)

At the same time, different investigative methods have been used to demonstrate convincingly that the decrease in quantity of all formed elements in the blood stream, including reticulocytes and erythrocytes, is governed by an exponential function [7-9].

We assumed that the decrease in reticulocytes occurs at a rate that is proportionate to the existing number of reticulocytes, i.e., the following function applies:

$$-\frac{dN_r}{dt} = \lambda N_r = \frac{0.693}{T_{\frac{1}{2}r}} \cdot N_r \qquad (4)$$

where $T_{\frac{1}{2}r}$ is the half-time for elimination of reticulocytes from the sample due to maturation, which equals the analogous parameter in the blood stream. From equation (4) we have the exponential law of change in number of reticulocytes as a function of time:

$$N_r = N_{r_0} e^{-\frac{0.693}{T_{\frac{1}{2}r}} t} \qquad (5)$$

For incubation, we took 1 m venous or capillary heparinized blood. Reticulocytes were counted in blood smears submitted to supravital staining with 1% brilliant cresyl blood solution. We counted all forms of reticulocytes encountered per 100,000 erythrocytes. We counted the reticulocytes in the blood sample before and 2, 3, 4 and 6 h after incubation.

According to equation (5), there is linear change in log $\frac{N_r}{N_{r_0}}$ as a function of time:

$$\log \frac{N_r}{N_{r_0}} = -\frac{0.3010}{T_{\frac{1}{2}r}} \cdot t \qquad (6)$$

On the basis of plotting relative number of reticulocytes N_r/N_{r_0}, expressed as a percentage, as a function of time on a semilogarithmic scale, as shown in Figure 1b, we used the least squares method to calculate half-time for elimination of reticulocytes $T_{\frac{1}{2}r}$ due to their maturation. Using equation (4), we calculated several more kinetic parameters of erythropoiesis (bone marrow production of reticulocytes and erythrocytes, as well as half-time for elimination of erythrocytes $T_{\frac{1}{2}er}$). Provided there is erythrocyte balance, the rate of reduction in reticulocytes determined with equation (4) is found to equal the production of these cells P_r per hour:

$$P_r = \frac{0.693}{T_{\frac{1}{2}r}} \cdot N_{r_0} \qquad (7)$$

Reticulocyte production scaled to 1 μℓ blood in 24 h, $P_r/_{day}$ can be determined with the following equation:

$$P_r/day = \frac{0.693 \cdot N_{r_0} \cdot N_{er} \cdot 24}{T_{\frac{1}{2}r} \cdot 1000} \qquad (8)$$

where N_{er} is the quantity of erythrocytes per μℓ blood. According to the exponential law of decrease in number of erythrocytes in the blood stream, we can determine daily production of erythrocytes per μℓ blood $P_{er/day}$ using the following equation:

$$P_{er/day} = \frac{0.693}{T_{\frac{1}{2}r}} \cdot N_{er} \qquad (9)$$

where $T_{\frac{1}{2}r}$ is the half-time for elimination of erythrocytes from the blood stream (in days). In the presence of erythrocyte balance, by equating reticulocyte and erythrocyte production, we can obtain an estimate of the half-time for elimination of erythrocytes:

$$T_{\frac{1}{2}er} = \frac{T_{\frac{1}{2}r}\cdot 1000}{N_{r_0}\cdot 24} \qquad (10)$$

Results and Discussion

The proposed method was used to determine erythrokinetic parameters of 14 healthy men. The results are listed in the Table (relative change in quantity of reticulocytes by 4th h of incubation N_r/N_{r_0}, half-time for elimination of reticulocytes and erythrocytes, erythrocyte production per day). A comparison of the obtained values for $T_{\frac{1}{2}er}$ to the results of direct determination by means of ^{51}Cr [10, 11] revealed that they coincide satisfactorily. The authors define the range of fluctuations as 24-42 days, with means of 26.5 and 29 days.

Results of determination of cytokinetic parameters of erythropoiesis in healthy people

Subject	N_{er} million /µℓ	N_{r0} ‰	N_{r4} ‰	ΔN_r according to Ye.N.Mosyagina	T_r, h according to Ye.N.Mosyagina	N_r/N_{r0}	$T_{\frac{1}{2}r}$, h	$T_{\frac{1}{2}r}$, days	Erythr. production thous (µℓ×day)
M-ov	5,00	16,37	11,54	4,83	13,5	0,705	8,2	20,9	166,0
A-ev	4,52	11,42	8,30	3,12	14,6	0,725	11,3	41,2	76,0
P-ov	4,46	13,68	10,66	3,02	18,1	0,780	10,8	32,9	94,0
G-ov	4,80	6,26	4,47	1,79	14,4	0,710	8,0	53,3	62,5
S-ko	4,69	8,57	6,52	2,05	16,7	0,760	7,7	37,5	86,1
N-ev	4,50	12,74	7,59	5,15	9,9	0,595	5,2	17,0	183,1
S-in	5,00	13,28	7,53	5,75	9,2	0,570	5,3	16,6	208,1
S-ov	4,51	9,80	8,40	1,40	28,0	0,84	10,3	43,8	71,4
M-ev	4,64	9,83	6,11	3,72	10,5	0,620	8,1	34,3	93,6
G-in	4,54	8,73	6,25	2,48	14,0	0,715	7,2	34,7	91,5
K-ov	4,68	15,85	12,05	3,80	16,7	0,790	7,2	16,8	193,0
Sh-ov	5,10	16,70	9,51	7,19	9,3	0,570	5,3	13,2	267,2
O-ov	5,00	6,24	3,32	2,92	8,6	0,530	4,7	29,6	110,4
F-ov	4,69	12,56	8,55	4,01	12,6	0,680	7,3	34,9	135,1
M	4,62	—	—	3,65	13,3	0,680	7,6	29,6	130,0
σ	0,19	—	—	1,7	5,7	0,076	1,90	11,7	60,0
m	0,05	—	—	0,47	1,6	0,021	0,53	3,2	15,7

The Table also lists data on reticulocyte content in the first and 4th hour of incubation, as well as erythrokinetic parameters determined by the method of Ye. N. Mosyagina (rate of maturation of reticulocytes proportionate to the difference $N_{r_0} - N_{r_4}$, period of maturation of reticulocytes). According to the hypothesis of Ye. N. Mosyagina that there is linear change in number of reticulocytes, with which the rate of their maturation has a certain definite value, we could have expected similar figures for change in quantity of reticulocytes in 4 h of incubation in all of the subjects. However, we observed, on the contrary, a wide range of variation of difference ΔN_r. The maximum value was 5 times greater than the minimum, while the mean coefficient of variation (σ/M) constituted 47%. A wide range of variation (3-fold) was also observed for the calculated period of reticulocyte maturation T_r, the coefficient of variation of which constituted 43%.

Conversely, with exponential decline in number of reticulocytes with a certain period of half-time of elimination thereof $T_{\frac{1}{2}r}$, we should expect similar values for $N_r \cdot N_{r_0}$. The data in the table confirm this. The maximum value of this ratio did not exceed by more than 1.5 times the minimum, while coefficient of variation γ constituted only 11%. A low coefficient of variation (25%) was also obtained for the half-time of reticulocyte elimination $T_{\frac{1}{2}r}$, which is indicative of the great stability of this erythrokinetic parameter, as compared to mean life span of reticulocytes.

We deem it possible to recommend the described method for clinical diagnostic and scientific studies in cases where the use of direct methods of testing cytokinetic parameters is impossible.

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MODIFICATION OF METHOD FOR ASSAYING OZONE BY THE DIACETYL DIHYDROLUTIDINE REACTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 12 Aug 80) pp 89-90

[Article by B. V. Anisimov, G. N. Kuz'menko and T. I. Golubeva]

[Text] Ozone is being studied intensively in two hygienic aspects: as the main toxic component of the atmosphere in photochemical smog and as a factor that is necessary in trace concentrations to assure the biological quality of the atmosphere of peopled premises wanting in "natural" air ventilation. The cockpits of spacecraft and other types of pressurized enclosures constitute such premises. For this reason, it is quite a pressing task to refine methods of measuring ozone.

Nash [1] proposed a specific method, but with low sensitivity, for measuring ozone, which is based on clearing a solution of diacetyl dihydrolutidine (DDL) using an initial concentration thereof of about 10^{-4} M and air aspiration rate of 0.5 ℓ/min. We tested the possibility of accelerating air aspiration and lowering the initial DDL concentration in the absorber solution to improve the sensitivity of the method.

We tested several types of diffuser-absorbers. The absorbers used by American authors--microimpingers [2]--were found unsuitable for this purpose. Satisfactory results were obtained only with the absorbers descrbed by E. V. Rykhter [3, 4]. Unlike the original design, the absorbers were made so that they could be taken apart. To prevent contact between ozone and the rubber and plastic tubes, the absorbers were interconnected by means of ground-glass joints. Three absorbers were connected to collect samples. Tests were made of two types of absorbers. The volume of DDL constituted 6 mℓ for absorbers of the first type (Figure 1) and 10 mℓ for the second type (Figure 2).

DDL was synthesized from the formula in the original article. Optical density was measured with an FEK-56M photocolorimeter with filter No 3, or spectrophotometer at 412 nm. The absorbent solution was prepared in 1/15 M phosphate buffer, pH 6.8, by diluting saturated DDL solution to optical density of 0.4, with a 2-cm working length of the cuvette [tray]. This optical density corresponds to a DDL concentration of $2.77 \cdot 10^{-5}$ M (molar extinction of DDL is 7700).

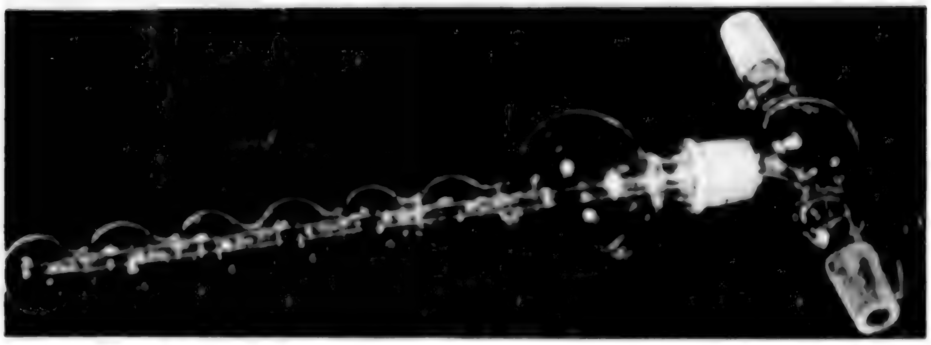

Figure 1. Small absorber

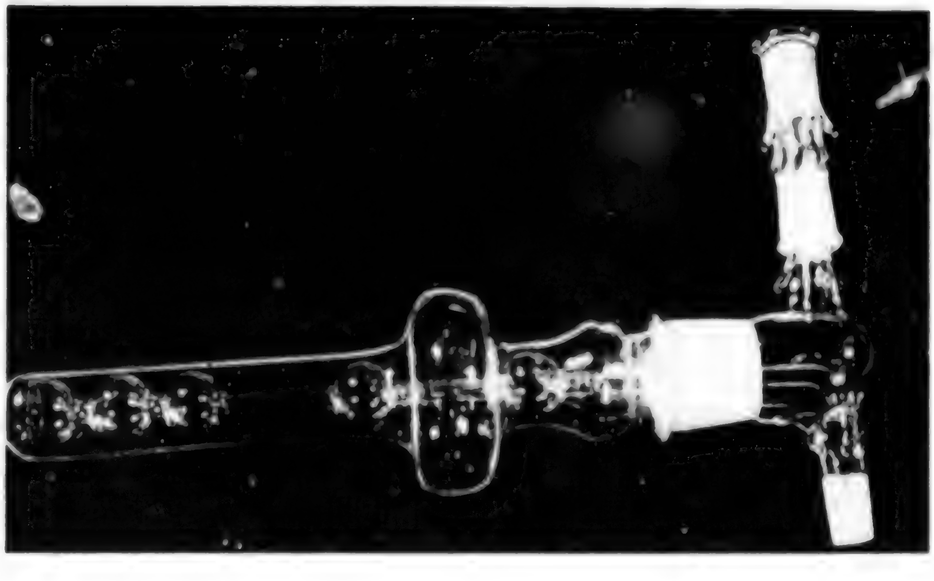

Figure 2. Large absorber

There was good absorption of ozone at bubbling rates of 3 to 5 ℓ/min in the small absorbers and 7 to 10 ℓ/min in the large ones. At these rates, passage of ozone into the next absorber did not exceed 3-5% until the optical density in the first absorber dropped to 0.25 and, accordingly, optical density of solution in the second absorber dropped by no more than 0.015-0.02, with consideration of adjustment for water evaporation.

Stoichiometric reaction of DDL with ozone in neutral buffer, 1:1. We estimated the amount of absorbed ozone in measuring optical density in a cuvette with working length of 2 cm in the following manner: it constituted (33.33 ΔD) μg with 10 mℓ absorbent solution and (20 ΔD) μg with 6 mℓ, where ΔD is reduction of optical density.

When samples are collected there is evaporation of absorbent solution. The correction for evaporation is calculated using the following formula:

$$D_{evap} = D_{alt} (B - \Delta B)/B$$

where D_{corr} is corrected [adjusted] optical density, D_{alt} is optical density of solution after taking a sample, B is mass or volume of absorbent with density of 1, ΔB is mass or volume loss of absorbent solution due to evaporation.

ΔD is defined as the difference, $D_0 - D_{evap}$, where D_0 is initial optical density of absorbent solution.

The proposed modification of the method increases sensitivity by 4 times by reducing the concentration of DDL solution. However, this is feasible only if one uses long microcuvettes with the spectrophotometer. In addition, the increase in rate of aspiratio reduces drastically sample collecting time. For example, using the above-mentioned volumes of absorbent, aspiration time is reduced to 15-20 min, versus 2-3 h, which are required in the original method for measuring the ozone concentration in the near-earth layer of air, i.e., to one-sixth-one-ninth [5].

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BRIEF REPORTS

UDC: 612.111.014.426

EFFECTS OF LOW-INTENSITY ELECTROMAGNETIC FIELDS ON HUMAN AND ANIMAL ERYTHROCYTES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 26 Dec 80) pp 91-92

[Article by V. P. Shabayev]

[Text] The objects of our study were balanced Locke-Ringer solution and human and albino rat blood erythrocyte suspensions (50% hematocrit) prepared with this solution. Blood was taken from animals after they were decapitated under ether anesthesia.

Changes in oxygen concentration and pH served as parameters characterizing the state of the aqueous medium. The concentration of oxygen in the samples was determined using a PPT-1 polarograph with open type platinum electrode at a temperature of 25±0.1°C. We used 0.1 M KCl as the calibrating solution; a pH-340 pH-meter was used to measure medium pH and records were made on an EPP-09.

We assessed permeability of erythrocyte membranes to water according to hemolysis in 0.47% NaCl. A previously developed technique [1] was used to obtain extracts of erythrocytes cultivated with and without shielding. The extracts were analyzed by means of disc electrophoresis [2]. The gels were stained with amido black 10-B for proteins.

A lead tent ($0.31 \times 0.16 \times 0.14$ m), the outer wall of which was made of ferromagnetic material ($4 \cdot 10^{-3}$ m thick), served as a shield to attenuate the electromagnetic field of earth. The attenuation of earth's EMF [electromagnetic field] was on the order of 100-200-fold, taking into consideration the openings in the walls of the shield [3]. Exposure time of specimens constituted 3 h in the ungrounded shield and ordinary conditions.

We assessed the effect of the shield from the difference between experimental and control data. We took 14 pairs of readings. Statistical reliability of the results was determined with Student's criterion ($P<0.05$ for biological experiments, $P<0.001$ for those with aqueous solutions) [4].

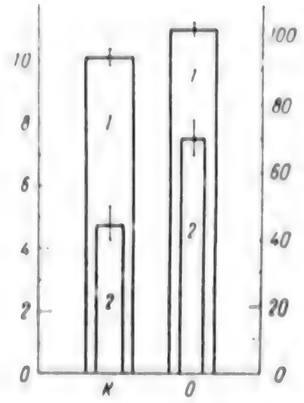

Figure 1.
Effect of electromagnetic shielding on O_2 content in Locke-Ringer solution (1) and osmotic hemolysis of rat erythrocytes (2) (n = 14). X-axis: K--control, O--under tent; y-axis: left--O_2 concentration (relative units), right--hemolysis (%)

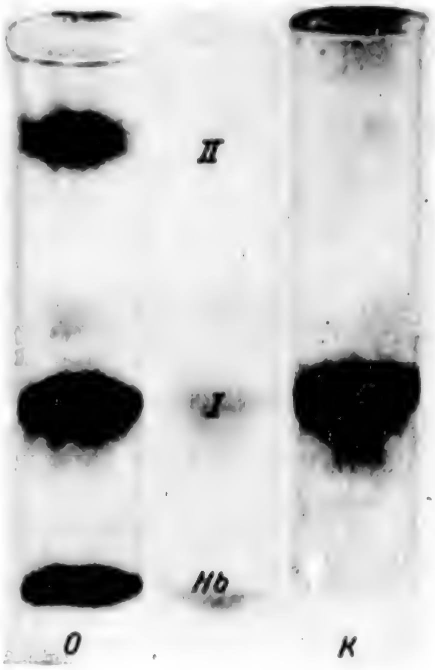

Figure 2.
Electrophoregrams of extracts obtained during incubation of human erythrocytes in diffuser [1] within 3 h. O--in tent; K--control

Results and Discussion

The data illustrated in Figure 1,*1* show that aqeuous Locke-Ringer solutions stored under an electromagnetic shield contain 8% more oxygen than the control. The cause of the shielding effect is unclear. However, it can be assumed that it was due to change in structural distinctions of water [5]. This hypothesis could be confirmed by the results of electrometric measurement of pH. The pH constituted 7.45±0.06 in the control Locke-Ringer solution and 7.25±0.08 ($P<0.05$) in the experiment.

As we know, water is a structural constituent of biological membranes [6] and intracellular contents [7]. For this reason, it is possible that the increase in osmotic and spontaneous hemolysis of erythrocytes contained under the shield is also attributable to structural changes in water of cells and interstitial regions (Figures 1,*2* and 2).

Since water is instrumental in conformation lability and organization of cell membranes [6, 7], we could expect release of biomacromolecules and complexes thereof into the intercellular regions. Figure 2 shows that with use of the shield (a), there is a large amount of hemoglobin and two other proteins (I, II) in the intercellular region, which are in the space near the cathode in electrophoresis. Interestingly enough, under ordinarly conditions (b), only one protein (I) is released from erythrocytes, which is probably involved in intercellular bonds and stabilizes the erythrocyte membrane [1].

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UDC: 612.352+612.744.11]-06:612.591

EFFECT OF HIGH AMBIENT TEMPERATURE ON CARBOHYDRATE METABOLISM IN RAT LIVER AND SKELETAL MUSCLES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 2 Mar 81) pp 92-94

[Article by R. Akhmedov and A. M. Nasyrova]

[Text] It is known that brief and prolonged exposure to high and low ambient temperatures leads to substantial changes in physiological reactions that maintain temperature homeostasis in organisms [1-6]. Adaptive changes in physiological functions are based on adaptive shifts in intensity of metabolism and energy [7-9]. In this regard, it is very interesting to investigate organic, tissular and cellular mechanisms of change in metabolism, the significance of the different elements of metabolism in different physiological systems of the body involved in maintaining temperature homeostasis with a changing ambient temperature.

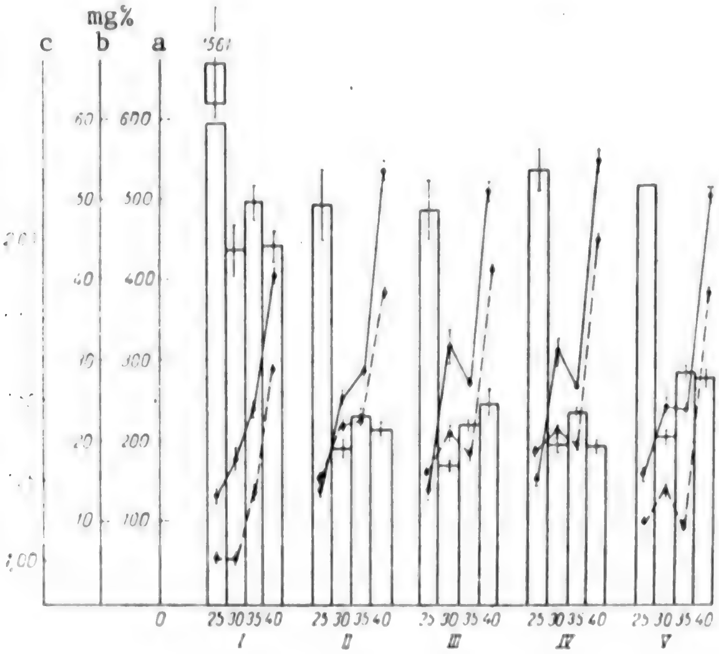
We have made an attempt here to demonstrate the distinctions of changes in carbohydrate metabolism in the liver and skeletal muscles related to exposure to high ambient temperatures, which flight personnel have occasion to encounter.

Methods

We had 120 mongrel albino rats of both sexes, weighing 140-200 g, in the experiment. The animals were exposed for 2 per day to high temperatures in a heat chamber for 3 days. The rats were divided into four groups: the first consisted of animals exposed to +30°C, the second to +35°C and the third to +40°C. The fourth group remained constantly at room temperature (20-25°C) and served as a control. We measured weight and rectal temperature of the rats before exposure to high temperatures and immediately after termination thereof. The animals were decapitated on the 3d day after termination of 2-h exposure. We rapidly excised liver and skeletal muscle tissues, which were cooled in liquid nitrogen for subsequent analysis of glycogen, lactic and pyruvic acid content. We used the anthrone method [10] to measure glycogen concentration in tissues, the method of Barker and Sammerson [11] to assay lactic acid and a modification of the Umbright method [11] for pyruvic acid. The obtained data were submitted to processing by the small samples method. Analysis is submitted with consideration of reliability of demonstrated changes ($P<0.05$).

Results and Discussion

The Figure illustrates the results of experiments, which were obtained with exposure of animals to different temperatures. The parameters characterizing tissular carbohydrate metabolism changed to different extents under the influence of different temperature levels. In all cases, regardless of ambient temperature, exposure of animals led to a decline of glycogen content in the liver and skeletal muscles. However, the degree of change differed in different organs, and it depended on ambient temperature. Thus, with exposure of animals to a temperature of 30°C the glycogen concentration in the liver dropped to almost one-fourth, and in different groups of skeletal muscles by 2.6-2.9 times.



Glycogen (white columns), lactic acid (solid line) and pyruvic acid (dash line) in the liver (I), masseter (II), thoracic (III), dorsal (IV) and femoral (V) skeletal muscles of rats exposed to different temperatures. X-axis, ambient temperature (°C); y-axis, glycogen (a), lactic acid (b) and pyruvic acid (c) levels (mg%)

Exposure of animals to higher temperature led to undulant change in glycogen content of the tissues of the organs examined. Thus, while the transition from 30°C to 35°C was associated with some elevation of glycogen level in tissues of different organs, exposure to 40°C led to another decline of this parameter. However, in this case too, the concentration of glycogen was still low, as compared to control data, and glycogen content of the liver was 67.8% lower in hepatic tissue and 43.7-55.1% lower in different groups of skeletal muscles at 35°C than the base level; at 40°C, the decline constituted 73.9 and 48-50%, respectively.

In contrast, exposure to different levels of heat led to rather drastic increase in lactate content of both hepatic tissue and different groups of skeletal muscles. The increment of lactate in tissues depended on the temperature. Thus, 2-h exposure to 30°C increased lactate of the liver by 54.1% and in skeletal muscles by 58.4-148.9%. The maximum increase was found in the thoracic muscle. At a temperature of 35°C, liver lactate content increased even more, by 117.1%, whereas the increase was less marked in various groups of skeletal muscles, and did not exceed 51.6-116.8%. Exposure of the animals to higher ambient temperature (40°C) led to drastic elevation of lactate levels in the tested organ tissues. It was 3.7 times higher than the base level in the liver and 2-3 times higher in skeletal muscles.

There was analogous change at these temperatures in pyruvate content, although it was less marked than lactate. In the temperature range of 30-35°C, the increase constituted 10.1-19.2% in the liver and 4.9-19.2% in skeletal muscles. The most distinct changes were demonstrated at a temperature of +40°C. In this case, the increment of pyruvate constituted 46.5% in the liver and 21-63% in various groups of skeletal muscles. The most appreciable increase in pyruvate was observed in thoracic, dorsal and femoral muscles (by 56.7-68.1%).

It should be noted that there was also elevation of the animals' temperature with increase in ambient temperature. While rectal temperature was 36.6°C at 20-25°C, it rose to 37.5°C at 30°C, 39.4°C at 35°C and 39.8°C at 40°C ambient temperature.

Thus, exposure of animals to different levels of high temperature was associated with a decline of glycogen level and elevation of lactic and pyruvic acid levels in the liver and skeletal muscles. There is some information in the literature on this score. Thus, several researchers reported an increase in lactic acid concentration in blood of rabbits, dogs, albino rats and chicks exposed to high temperatures, and the increment was a function of temperature [12-14]. Analogous results were obtained in our experiments, where we assayed lactic acid in the liver and skeletal muscles. However, we were impressed by the dissimilar changes in glycogen content of the tissues examined. The most appreciable change was demonstrated in the liver. Apparently, heat alters to different degrees the intensity of carbohydrate metabolism in different body tissues. All these data are indicative of intensification of glycolytic processes in tissues of different organs with exposure to high ambient temperature. The causes of faster glycolysis at high temperature have not yet been determined. Perhaps it is attributable to elevation of temperature of the tissues themselves as a result of hyperthermia. Indeed, rectal temperature rose appreciably when the animals were exposed to high ambient temperature, and the increment depended on the temperature level. This phenomenon may also be related to hemodynamic changes as a result of thermoregulatory redistribution of blood in the nucleus and membrane [15]. Such redistribution could lead to hypoxia and, consequently, activation of anaerobic energy production.

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DISCUSSIONS

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VIBRATION AND ASSESSMENT OF THIS FLIGHT FACTOR BY PILOTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 16, No 3, May-Jun 82 (manuscript received 16 Mar 81) pp 94-96

[Article by Yu. N. Kamenskiy]

> [Text] The author of the following article, which deals with vibration as one of the active factors in the pilot-helicopter-environment system, not only notes the deleterious effect of this factor on pilot performance, but stresses its role as a source of information about the status of the helicopter and its systems. To date, sufficient material has been accumulated in aviation medicine to confirm the role of noninstrument information (angular and longitudinal accelerations, vibration, noise, etc.) in piloting an aircraft (higher precision of control, recognition of emergency situations, etc.). For this reason, we consider that there is validity to the author's idea about special-purpose pilot training in the use of such "negative" flight factors as vibration, buffeting as information about the status of the vehicle they are to control. As for consideration of the informative value of vibrational stimuli, when standards are set for them, comprehensive studies are required for practical use thereof. [Commentary by editorial board]

The effectiveness of controlling any equipment, in particular transport equipment, depends not only on conformity of the equipment's specifications to man's physiological capabilities. The industrial [work] environment has a strong influence on the control process. This influence may be direct or mediated by changes in functional state of the body and decline of the operator's work capacity [1-3]. In this regard, such a powerful environmental factor as vibration plays a special part [4-6]. If this factor is generated by the controlled equipment itself, it should be considered a technical feature of the machine, which must conform to the physiological and mental capabilities of the operator. However, aviation ergonomics does not yet take into sufficient consideration the role of vibration in the man-aircraft system.

Our objective here was to assess the role of vibration in the pilot-helicopter system, on the basis of the estimates of the pilots themselves.

Methods

The anonymous questionnaire method was used to interrogate 116 helicopter crew members. The questionnaire was specially prepared for this study and consisted of 36 questions and multiple choice answers. The subject was to underline the answer that corresponded best to his opinion after reading the question. Some of the questions required a yes or no answer and some provided for giving a so-called free answer.

Results and Discussion

The absolute majority of interrogated pilots (86%) consider vibration to be the most unpleasant factor in the helicopter cabin (even more unpleasant than noise; 58%). Subjectively, vibration is perceived by 82% of the pilots as continuous rhythmic tremor that is transmitted the most to the trunk (58%) and head (30%). Such perception of vibration is objectively attributable to the fact that the frequency of helicopter oscillations is a multiple of the number of blades and revolutions of the rotor [7]. For this reason, the vibration of a helicopter approximates orderly polyharmonic oscillations.

Prolonged vibration during the flight shift caused fatigue in 70% of the pilots, which started to be manifested after flying for 3-5 h; 8% reported unpleasant sensations and 14% irritation.

The pilots observed the most intensive vibration at take-off (40%), when flying with cargo suspended outside (34%) and particularly when landing (88%), which is related to the phenomenon of so-called earth's resonance [7].

Helicopter vibration makes it difficult to read the instruments, particularly during landings (74%). It is difficult to take information from virtually all of the instruments, particularly the rotor and engine revolution indicators (55%). This can be attributed to the indistinctness of hands and numerals on the instruments (68%) and more intensive oscillation of needles (22%) due to vibration. The consequent reading errors could reach 20-50% [8].

In the opinion of 34% of the pilots, the difficulty involved in reading the instruments make it more difficult to pilot the helicopter. In order to read the instruments better, 44% of the pilots are compelled to draw their head close to the instrument panel (to a distance of about 50 cm), for which they must lean forward. Such a position is uncomfortable and could lead to premature fatigue of postural muscles [9].

Eye strain related to vibration interference in reading instruments elicits eye fatigue, which is reported by 64% of the pilots. This involves decrease in resolution of the visual analyzer, greater number of mistakes when tracking a moving object [10]. Vibration also makes it difficult to perceive objects outside the cabin (34%), including observation of cargo suspended outside (14%).

In the opinion of 56% of the pilots, vibration makes it difficult to control the helicopter, since it causes strain of skeletal muscles (44%) and reduces accuracy of controlling movements (26%). Vibration makes it the most difficult to work the pedals and "pitch-throttle" lever, which occurs the most often at such an important phase of the flight as landing (70%) and when flying with cargo suspended outside (40%).

Apparently, vibration plays some part in occurrence of inflight spatial illusions, which were reported by 42% of the pilots: 20% during landings, 16% during instrument flights and 28% when visibility was poor. More than half the pilots who reported illusions did not directly relate them to vibrations, considering them to be the conseuqence of fatigue, while the others had difficulty in determining the cause of illusions. In view of the fact that vibration causes fatigue, this factor can be considered one of the indirect causes of spatial illusions. In addition, it is known that long-term exposure to low-frequency vibration diminishes sensibility of the vestibular system [11]. This is associated with impaired spatial perception [12]; consequently, vibration may also be the immediate cause of illusions in the pilots.

Thus, helicopter vibration plays a negative role in the pilot-helicopter system, making it more difficult to fly the craft and lowering pilot reliability. The adverse effect is manifested the most during landings, particularly at the end of the flight shift, when the pilots develop fatigue. Apparently, these factors are among the causes of the high helicopter accident rate during landings [13].

At the same time, we know that vibration in the man-machine system also plays a positive role as a source of noninstrumental information [14, 15]. In the pilots' opinion, vibration contains useful information about the state of the helicopter as a whole (24%), about operation of the engines (10%), main (44%) and tail rotors (4%), flying mode (30%). The level of informativeness was little-related to the means of transmission of vibration to the pilot: floor vibration is considered the most informative by 26% of the pilots, chair vibration by 32%, controls by 36% and instrument panels 22%. This is apparently due to the fact that the low-frequency vibration of the helicopter is poorly damped by both structural elements and human body tissues, and it is perceived by all parts of the body, regardless of where it is applied.

From the standpoint of obtaining information, 80% of the pilots consider the level of vibration to be excessive; 82% deem it necessary to reduce vibration significantly in crew's cabins, but not eliminate it entirely. Evidently, when setting standards for vibration in helicopter crew cabins, one should take into consideration the significance of vibration as a source of noninstrumental information.

However, vibration can also be used as a source of instrumental information by pilots. In aviation, the problem of relieving the visual analyzer of pilots and providing for greater reliability of their perception of instrument information is becoming increasingly acute [16]. In this situation, it is deemed important to search for new channels for transmitting information to pilots. In the opinion of a number of researchers, a vibrotactile channel is the most promising in this regard [17, 18]. Helicopter pilots believe that information about some parameters, particularly air speed, can be displayed on vibration indicators. Trials of a vibration channel to relay information to pilots revealed that the time of correcting deviations of monitored parameters decreased from 0.65 to 0.43 s [19].

Consequently, vibration is an important factor in the pilot-helicopter system. On the one hand, vibration makes the flying process more difficult and lowers pilot work capacity; on the other hand, it is a source of information about the state of the helicopter or its different systems. Such duality leads to dual solution of the problem--as a special "pilot and vibration" problem and as a more general "operator and vibration" problem. Apparently, it is necessary to settle the matter of the vibration factor in man-machine systems. This process should follow, first of all, the route of lowering the intensity of vibration at its source and along its paths. And one must not overlook the informative role of vibration in man-machine systems.

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